LEK. SZYMON JONIK

„KARDIOGRUPA – WYNIKI KWALIFIKACJI W REFERENCYJNYM OŚRODKU AKADEMICKIM"

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu

w dyscyplinie nauki medyczne

Promotor: dr hab. n. med. Tomasz Mazurek

Promotor pomocniczy: dr. n. med. Michał Marchel

I Katedra i Klinika Kardiologii

Warszawski Uniwersytet Medyczny

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RODZICOM: KRYSTYNIE I EUGENIUSZOWI

SPIS TREŚCI

1. WYKAZ PUBLIKACJI STANOWIĄCYCH PRACĘ DOKTORSKĄ

- Jonik Szymon, Marchel Michał, Pędzich-Placha Ewa, Pietrasik Arkadiusz, Rdzanek Adam, Huczek Zenon, Kochman Janusz, Scisło Piotr, Czub Paweł, Wilimski Radosław, Hendzel Piotr, Opolski Grzegorz, Grabowski Marcin, Mazurek Tomasz. Heart Team for Optimal Management of Patients with Severe Aortic Stenosis—Long-Term Outcomes and Quality of Life from Tertiary Cardiovascular Care Center. *Journal of Clinical Medicine* 2021; 10(22): 5408. doi: 10.3390/jcm10225408.

- Jonik Szymon, Marchel Michał, Pędzich-Placha Ewa, Pietrasik Arkadiusz, Rdzanek Adam, Huczek Zenon, Kochman Janusz, Budnik Monika, Piątkowski Radosław, Scisło Piotr, Kochanowski Janusz, Czub Paweł, Wilimski Radosław, Hendzel Piotr, Grabowski Marcin, Filipiak Krzysztof Jerzy, Opolski Grzegorz, Mazurek Tomasz. Long-term outcomes and quality of life following implementation of dedicated mitral valve Heart Team decisions for patients with severe mitral valve regurgitation in tertiary cardiovascular care center. *Cardiology Journal* 2022; Mar 14. doi: 10.5603/CJ.a2022.0011. Online ahead of print.

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2. SPIS RYCIN

3. WYKAZ SKRÓTÓW (alfabetycznie)

1-VD – one-vessel disease, jednonaczyniowa choroba wieńcowa

2-VD – two-vessel disease, dwunaczyniowa choroba wieńcowa

3-VD – three-vessel disease, trójnaczyniowa choroba wieńcowa

ACS – acute coronary syndrome, ostry zespół wieńcowy

AF – atrial fibrillation, migotanie przedsionków

AKI – acute kidney injury, ostre uszkodzenie nerek

AS – aortic stenosis, zwężenie zastawki aortalnej

AVAi – indexed aortic valve area, indeksowane pole zastawki aortalnej

BARC – The Bleeding Academic Research Consortium

CABG – coronary artery bypass grafting, pomostowanie aortalno-wieńcowe

COPD – chronic obstructive pulmonary disease, przewlekła obturacyjna choroba płuc

CTA – computed tomography angiography, angiotomografia

CTO – chronic total occlusion, przewlekła okluzja tętnicy wieńcowej

CV – cardiovascular, sercowo-naczyniowy

DVI – doppler velocity index, spoczynkowy wskaźnik bezwymiarowy

ERO – effective regurgitant orifice, efektywne pole powierzchni niedomykalności

EuroSCORE II – European System for Cardiac Operative Risk Evaluation II, skala EuroSCORE II

FFR – fractional flow reserve, pomiar cząstkowej rezerwy przepływu wieńcowego

HT – Heart Team, kardiogrupa

IVUS – intravascular ultrasound, ultrasonografia wewnątrzwieńcowa

LAD – left anterior descending, gałąź przednia zstępująca lewej tętnicy wieńcowej

LM – left main, pień lewej tętnicy wieńcowej

LVEDD – left ventricular end-diastolic diameter, wymiar końcoworozkurczowy lewej komory

LVEF – left ventricular ejection fraction, frakcja wyrzutowa lewej komory

MACCE – major adverse cardiac and cerebrovascular events, poważne zdarzenia sercowe i sercowo-naczyniowe

MC – MitraClip, korekcja niedomykalności mitralnej z użyciem systemu MitraClip

MCS – mental component summary, komponenta psychiczna jakości życia

MI – myocardial infarction, zawał serca

MR – mitral regurgitation, niedomykalność mitralna

MVD – multivessel disease, wielonaczyniowa choroba wieńcowa

MVG – mitral valve gradient, gradient mitralny

MVR – mitral valve replacement, wymiana zastawki mitralnej

NSTEMI – non-ST segment elevation myocardial infarction, zawał serca bez uniesienia odcinka ST

NYHA – New York Heart Association, skala New York Heart Association

OMT – optimal medical therapy, optymalna terapia medyczna

pAVG – peak aortic valve gradient, maksymalny gradient aortalny

PCI – percutaneous coronary intervention, przezskórna interwencja wieńcowa

PCS – physical component summary, komponenta fizyczna jakości życia

PH – pulmonary hypertension, nadciśnienie płucne

PTAV – percutaneous transluminal aortic valvuloplasty, przezskórna walwuloplastyka aortalna

SAVR – surgical aortic valve replacement, chirurgiczna wymiana zastawki aortalnej

SD – standard deviation, odchylenie standardowe

STEMI – ST-segment elevation myocardial infarction, zawał serca z uniesieniem odcinka ST

STS – Society of Thoracic Surgeons, skala Society of Thoracic Surgeons

STS-PROM - Society of Thoracic Surgeons Predicted Risk of Mortality, skala Society of Thoracic Surgeons Predicted Risk of Mortality

TAVR – transcatheter aortic valve replacement, przezcewnikowa wymiana zastawki aortalnej

TEER – transcatheter edge-to-edge repair, przezcewnikowa naprawa zastawki mitralnej

TIA – transient ischemic attack, przemijający epizod niedokrwienny

UA – unstable angina, niestabilna dławica piersiowa

4. KARDIOGRUPA – WYNIKI KWALIFIKACJI W REFERENCYJNYM OŚRODKU AKADEMICKIM [STRESZCZENIE]

Koncepcja kardiogrupy (ang. Heart Team) jako zespołu specjalistów podejmujących optymalne decyzje terapeutyczne u pacjentów z wielonaczyniową chorobą wieńcową lub zastawkową wadą serca ma ugruntowaną pozycję w rekomendacjach zarówno europejskich, jak i amerykańskich towarzystw kardiologicznych. Multidyscyplinarne podejście, uwzględniające dane kliniczne, angiograficzne i echokardiograficzne, ryzyko powikłań okołozabiegowych, rokowanie krótkoterminowe i odległe oraz preferencje chorego wydaje się być najbardziej racjonalnym narzędziem decydującym o wyborze optymalnej strategii postępowania dla tych „trudnych" pacjentów, obciążonych wieloma chorobami współtowarzyszącymi, nierzadko w podeszłym wieku, z procesem nowotworowym lub zespołem kruchości. Również w I Katedrze i Klinice Kardiologii Warszawskiego Uniwersytetu Medycznego, referencyjnym trzeciorzędowym ośrodku akademickim, od 2016 roku, cotygodniowo, odbywają się konsylia kardiologów, kardiochirurgów, echokardiografistów i specjalistów wielu innych dziedzin medycyny, mające na celu prezentację chorych oraz wspólną dyskusję i wybór optymalnego sposobu dalszego postępowania terapeutycznego. W latach 2016-2019 podczas 176 posiedzeń kardiogrupy przedstawiono 1925 pacjentów z zaawansowaną chorobą wieńcową, zwężeniem zastawki aortalnej lub niedomykalnością zastawki mitralnej, wybierając dla tych chorych jedną z trzech głównych opcji leczenia: kardiochirurgiczne, przezskórne lub zachowawcze. Charakterystykę kliniczną, dane echokardiograficzne i angiograficzne oraz wyniki kwalifikacji pacjentów konsultowanych w latach 2016-2019 zgromadzono retrospektywnie, a następnie poddano dalszej obserwacji (follow-up), oceniając powikłania okołozabiegowe, zdarzenia sercowo-naczyniowe w perspektywie krótkoterminowej i odległej, a także jakość życia chorych w zależności od wdrożonej strategii leczenia. Następnie przeprowadzono analizę statystyczną, wykreślając krzywe Kaplana-Meiera obrazujące śmiertelność i występowanie zdarzeń sercowo-naczyniowych w obserwacji długoterminowej dla pacjentów leczonych kardiochirurgicznie, przezskórnie lub zachowawczo, oraz porównano zastosowane strategie terapeutyczne między sobą.

W pierwszej publikacji dotyczącej funkcjonowania kardiogrupy w I Katedrze i Klinice Kardiologii Warszawskiego Uniwersytetu Medycznego przedstawiono charakterystykę kliniczną i echokardiograficzną oraz oceniono występowanie zdarzeń sercowo-naczyniowych i jakość życia pacjentów z ciężkim objawowym zwężeniem zastawki aortalnej, zakwalifikowanych przez specjalistów Heart Teamu do jednej z trzech metod leczenia: kardiochirurgicznej wymiany zastawki aortalnej (SAVR, surgical aortic valve replacement) wraz z optymalną terapią medyczną (OMT – optimal medical therapy) – SAVR+OMT, przezcewnikowej wymiany bioprotezy aortalnej (TAVR, transcatheter aortic valve replacement) wraz z optymalną terapią medyczną – TAVR+OMT lub jedynie optymalnej terapii medycznej – OMT.

W latach 2016-2019 podczas 176 posiedzeń kardiogrupy konsultowano 656 chorych ze zwężeniem zastawki aortalnej, a ostatecznie (po wykluczeniu pacjentów niespełniających kryteriów badania) do końcowej analizy włączono 482 chorych z ciężkim objawowym zwężeniem zastawki aortalnej, których zakwalifikowano, a następnie leczono zgodnie z decyzją kardiogrupy: kardiochirurgicznie (SAVR+OMT) – 85 pacjentów, przezskórnie (TAVR+OMT) – 318 pacjentów lub zachowawczo (OMT) – 79 pacjentów. Mediana okresu obserwacji wyniosła 866 dni.

Chorzy zakwalifikowani do strategii OMT byli najstarsi (81,7±8,0 lat) oraz prezentowali najbardziej nasilone objawy niewydolności serca (ocenione za pomocą skali NYHA – New York Heart Association), $p<0,01$; blisko 75% z nich miało cechy zespołu kruchości, byli najbardziej obciążeni występowaniem większości chorób współtowarzyszących, a ponadto ich ryzyko okołozabiegowe oszacowane w skalach EuroSCORE II (European System for Cardiac Operative Risk Evaluation II) i STS score (Society of Thoracic Surgeons score) było najwyższe, $p<0,01$.

Wszyscy pacjenci byli ocenieni echokardiograficznie – w grupie OMT przed konsultacją kardiogrupy; w kohortach SAVR i TAVR – przed konsultacją kardiogrupy oraz po zastosowanym leczeniu zabiegowym. Ewaluacja echokardiograficzna przed konsultacją kardiogrupy wykazała istotne statystycznie różnice w następujących parametrach: frakcji wyrzutowej lewej komory (LVEF, left ventricular ejection fraction) i częstości występowania dwupłatkowej zastawki aortalnej, które były najwyższe w grupie SAVR (odpowiednio – 56,5±12,1% i 13 (15,3%), $p<0,05$) oraz ciężkości zwężenia zastawki aortalnej ocenionej jako pole zastawki aortalnej indeksowane na metr kwadratowy (m^2) powierzchni ciała (AVAi, indexed aortic valve area) – najniższej w grupie TAVR (0,45±0,16 cm^2/m^2, $p<0,01$). Ocena pozabiegowa wykazała istotną statystycznie poprawę w zakresie parametrów echokardiograficznych: wymiaru końcoworozkurczowego lewej komory (LVEDD, left ventricular end-diastolic diameter), spoczynkowego wskaźnika bezwymiarowego (DVI, doppler velocity index) oraz maksymalnego gradientu aortalnego (pAVG, peak aortic valve gradient) u pacjentów leczonych kardiochirurgicznie, $p<0,01$.

Jako złożony pierwszorzędowy punkt końcowy oceniano wystąpienie zgonu z jakiejkolwiek przyczyny, niezakończonego zgonem udaru mózgu powodującego niepełnosprawność lub niezakończonej zgonem powtórnej hospitalizacji z powodu zwężenia zastawki aortalnej i jego najwyższy statystycznie odsetek odnotowano w grupie OMT (94,9% vs. 32,9% – SAVR i 34,6% –

TAVR, p<0,01). Ponadto, wystąpienie drugorzędowych punktów końcowych zaobserwowano istotnie statystycznie rzadziej w kohortach SAVR i TAVR niż u chorych leczonych zachowawczo (p<0,05). Porównując wyłącznie strategie inwazyjne – u pacjentów z grupy TAVR odnotowano mniejszy odsetek występowania ostrego uszkodzenia nerek (AKI, acute kidney injury), nowo rozpoznanego migotania przedsionków (AF, atrial fibrillation) oraz poważnego krwawienia zdefiniowanego jako ≥ 3 według skali BARC (The Bleeding Academic Research Consortium), p<0,05. Z kolei, w grupie SAVR obserwowano istotnie statystycznie niższy odsetek poważnych powikłań naczyniowych i konieczności implantacji stymulatora serca (PP, permanent pacemaker), p<0,05. Nie odnotowano natomiast istotnych statystycznie różnic pomiędzy kohortami SAVR i TAVR, jeśli chodzi o występowanie pierwszorzędowego punktu końcowego i pozostałych drugorzędowych punktów końcowych. Śmiertelność wewnątrzszpitalna nie różniła się pomiędzy strategiami interwencyjnymi (6 (7,1%) – SAVR vs. 20 (6,3%) – TAVR, p=0,80), podczas gdy długość pobytu w oddziale intensywnej terapii lub intensywnego nadzoru kardiologicznego była istotnie wydłużona u chorych leczonych kardiochirurgicznie (4,2±3,7 dni dla SAVR vs. 1,8±3,8 dni dla TAVR, p<0,05).

Jakość życia pacjentów (oceniona z użyciem kwestionariusza SF-36) – zarówno komponenty: fizyczna (PCS, physical component summary), psychiczna (MCS, mental component summary), jak i całkowita nie różniły się w kohortach SAVR, TAVR i OMT podczas kwalifikacji kardiogrupy (p>0,01), natomiast na zakończenie obserwacji długoterminowej chorzy, których leczono jedynie zachowawczo oceniali swoją jakość życia – fizyczną, psychiczną i całkowitą gorzej niż pacjenci leczeni kardiochirurgicznie lub przezskórnie (p<0,01). Nie zaobserwowano różnic istotnych statystycznie w jakości życia pacjentów, których zgodnie z kwalifikacją kardiogrupy poddano leczeniu interwencyjnemu (SAVR lub TAVR).

W przedstawionym artykule pokazaliśmy, że po uważnej kwalifikacji doświadczonych członków kardiogrupy, a następnie starannym wdrożeniu podjętych decyzji, strategie inwazyjne zapewniają lepsze długoterminowe wyniki leczenia i poprawiają jakość życia pacjentów z ciężkim objawowym zwężeniem zastawki aortalnej.

W kolejnym artykule przedstawiliśmy charakterystykę kliniczną i echokardiograficzną, wyniki kwalifikacji kardiogrupy oraz długoterminowe wyniki leczenia i jakość życia pacjentów z ciężką objawową niedomykalnością zastawki mitralnej. Chorych podczas posiedzeń Heart Teamu zakwalifikowano, a następnie leczono z wykorzystaniem jednej ze strategii terapeutycznych: kardiochirurgiczną wymianą zastawki mitralnej (MVR, mitral valve replacement) wraz z optymalną terapią medyczną – MVR+OMT, przezskórną korekcją niedomykalności mitralnej (TEER – transcatheter edge-to-edge repair) z użyciem systemu MitraClip (MC) wraz z optymalną terapią medyczną – MC+OMT lub jedynie zachowawczo – OMT.

W latach 2016-2019 podczas 176 posiedzeń kardiogrupy omówiono 254 chorych z niedomykalnością zastawki mitralnej, a ostatecznie w końcowej analizie (uwzględniając kryteria włączenia i wyłączenia) przeprowadzono ewaluację 157 pacjentów z ciężką objawową niedomykalnością mitralną, których zakwalifikowano do MVR+OMT – 46 chorych, MC+OMT – 58 chorych lub OMT – 53 chorych. Średni okres obserwacji (SD) w przypadku tej grupy wynosił 29±15 miesięcy.

Jeśli chodzi o istotne statystycznie różnice w charakterystyce klinicznej, pacjenci z kohorty OMT byli najstarsi (73,7±11,05 lat), charakteryzowali się najwyższą koincydencją cukrzycy (64,2%), migotania przedsionków (41,5%) i przewlekłej obturacyjnej choroby płuc (COPD, chronic obstructive pulmonary disease) – 43,4%, p<0,05; wśród chorych zakwalifikowanych do leczenia kardiochirurgicznego stwierdzono największy odsetek pierwotnej (organicznej) etiologii niedomykalności mitralnej (56,5%) oraz najniższe ryzyko okołozabiegowe ocenione według skali EuroSCORE II, p<0,05; pacjenci z grupy MC byli najczęściej obciążeni współistniejącą przewlekłą chorobą nerek (94,8%) oraz wywiadem uprzedniego pomostowania aortalno-wieńcowego (29,3%); chorzy ci byli też najbardziej objawowi jeśli chodzi o symptomy niewydolności serca (ocena według skali NYHA), p<0,05.

Również dla wszystkich pacjentów z ciężką niedomykalnością mitralną przedstawionych podczas posiedzeń kardiogrupy, w prezentowanym poniżej artykule podaliśmy pełne dane echokardiograficzne. Chorzy zakwalifikowani do MVR, MC lub OMT różnili się istotnie, jeśli chodzi o LVEF – najwyższa w kohorcie MVR (42,4±6,1%) oraz LVEDD i efektywne pole powierzchni niedomykalności (ERO, effective regurgitant orifice) – najniższe w kohorcie MVR (odpowiednio: 6,24±0,65 cm i 0,37±0,08 cm^2), oraz średni gradient mitralny (mean MVG, mean mitral valve gradient) – najniższy w grupie MC (4,12±1,41 mmHg), p<0,05. Natomiast ocena pozabiegowa (po MVR lub MC) wykazała istotnie statystycznie większą poprawę w zakresie odsetka resztkowej centralnej fali niedomykalności ≥ 2 stopnia i przecieku okołozastawkowego oraz wartości ERO, objętości zwrotnej fali mitralnej (MR volume) oraz maksymalnego i średniego gradientu mitralnego w grupie chorych leczonych kardiochirurgicznie w porównaniu do korekcji przezskórnej z użyciem MC (p<0,05).

Śmiertelność wewnątrzszpitalna nie różniła się istotnie pomiędzy grupami zakwalifikowanymi do postępowania inwazyjnego (4 (8,7%) vs. 1 (1,7%), MVR vs. MC, p=0,10). Jeśli chodzi o wystąpienie pierwszorzędowego punktu końcowego (zgon z przyczyn sercowo-naczyniowych), zaobserwowano go najczęściej w kohorcie pacjentów leczonych zachowawczo (20 (37,7%)), podczas gdy dla MVR i MC wynosił odpowiednio – 7 (15,2%) i 10 (17,2%), p=0,01. Ponadto, również w przypadku drugorzędowych punktów końcowych (zgon z jakiejkolwiek przyczyny, niezakończony zgonem zawał serca, niezakończony zgonem udar mózgu, niezakończona zgonem hospitalizacja z powodu zaostrzenia objawów niewydolności serca lub sumaryczny odsetek zdarzeń sercowo-naczyniowych) ich częstość była niższa w grupach chorych leczonych kardiochirurgicznie lub przezskórnie w porównaniu ze strategią zachowawczą ($p<0,05$). Porównując jedynie strategie interwencyjne, MVR i MC nie różniły się istotnie statystycznie, jeśli chodzi o odsetek występowania pierwszorzędowego i drugorzędowych punktów końcowych ($p>0,05$).

Jakość życia chorych (oceniona z użyciem kwestionariusza SF-36) – zarówno komponenty: PCS, MCS, jak i całkowita nie różniły się w kohortach MVR, MC i OMT podczas kwalifikacji kardiogrupy ($p>0,05$), natomiast na koniec obserwacji długoterminowej chorzy z grupy leczonej zachowawczo oceniali swoją jakość życia – fizyczną, psychiczną i całkowitą jako najgorszą ($p<0,01$).

W tej publikacji również wykazaliśmy znaczącą rolę kardiogrupy w podejmowaniu decyzji terapeutycznych u pacjentów z ciężką objawową niedomykalnością zastawki mitralnej. Staranna ocena, a następnie implementacja podjętych decyzji przez doświadczony zespół kardiologiczno-kardiochirurgiczny skutkowały lepszymi wynikami leczenia i poprawą jakości życia u chorych zakwalifikowanych do postępowania inwazyjnego – zarówno kardiochirurgicznego, jak i przezskórnego.

W ostatnim artykule oryginalnym tworzącym cykl publikacji przedstawiono wyniki konsultacji kardiogrupy u pacjentów z zaawansowaną chorobą wieńcową (zdefiniowaną jako choroba trójnaczyniowa (3-VD, three-vessel disease) i/lub ekwiwalent choroby wielonaczyniowej – istotne (≥50%) zwężenie pnia lewej tętnicy wieńcowej (LM disease, left main disease)); przedstawiono charakterystykę kliniczną, echokardiograficzną i angiograficzną oraz oceniono występowanie powikłań, zdarzeń sercowo-naczyniowych i jakość życia chorych po implementacji decyzji Heart Teamu.

W latach 2016-2019 podczas 176 posiedzeń kardiogrupy konsultowano 1509 chorych z chorobą wieńcową. Ostatecznie do końcowej analizy (po wykluczeniu pacjentów niespełniających kryteriów badania opisanych powyżej) włączono 1286 chorych z zaawansowaną chorobą wieńcową, których zakwalifikowano do leczenia kardiochirurgicznego – pomostowania aortalno-wieńcowego (CABG, coronary artery bypass grafting) wraz z optymalną terapią medyczną – CABG+OMT (356 chorych), przezskórnego – przezskórnej interwencji wieńcowej (PCI, percutaneous coronary intervention) wraz z optymalną terapią medyczną – PCI+OMT (679 chorych) lub jedynie zachowawczego – OMT (251 chorych). Jako pierwszorzędowy złożony punkt końcowy zdefiniowano sumę poważnych zdarzeń sercowo-naczyniowych (MACCE, major adverse cardiac or cerebrovascular events) – zgon z jakiejkolwiek przyczyny, zawał serca, udar mózgu lub ponowną rewaskularyzację wieńcową. Powyższe komponenty rozpatrywane oddzielnie, a także sumaryczny odsetek zgonu z jakiejkolwiek przyczyny, zawału serca lub udaru mózgu, zgon sercowo-naczyniowy, zgon wewnątrzszpitalny, udar mózgu zakończony niepełnosprawnością; ponadto – dla chorych leczonych interwencyjnie – zakrzepica w stencie lub okluzja graftu zostały zdefiniowane jako drugorzędowe punkty końcowe. Średni okres obserwacji w przypadku tej grupy wynosił 37±14 miesięcy.

Blisko 41% pacjentów omawianych podczas posiedzenia kardiogrupy było hospitalizowanych z rozpoznaniem ostrego zespołu wieńcowego (ACS, acute coronary syndrome): świeżego zawału serca z uniesieniem odcinka ST (STEMI, ST-segment elevation myocardial infarction) lub bez uniesienia odcinka ST (NSTEMI – non-ST segment elevation myocardial infarction) lub niestabilnej dławicy piersiowej (UA, unstable angina), 3,4% było we wstrząsie kardiogennym, a pozostali prezentowani chorzy mieli rozpoznany przewlekły zespół wieńcowy. Obserwowano istotne statystycznie różnice w charakterystyce klinicznej – pacjenci zakwalifikowani przez kardiogrupę jedynie do leczenia zachowawczego byli najstarsi (72,5±9,9 lat) i blisko 2/3 z nich miało cechy zespołu kruchości, p<0,01. Ponadto chorzy z kohorty OMT najczęściej mieli rozpoznaną niewydolność serca (92%) i prezentowali symptomy ciężkiej objawowej niewydolności serca w klasie NYHA III-IV (51,4%), ciężkie upośledzenie funkcji skurczowej lewej komory serca – LVEF < 30 % (57%), istotnie zwiększony LVEED (6,2±1,0 cm) i byli w największym odsetku obciążeni migotaniem przedsionków (37,8%), przewlekłą chorobą nerek (76,9%), niedokrwistością (62,5%), ciężkim nadciśnieniem płucnym (PH, pulmonary hypertension) – 13,9% i wywiadem nowotworowym (35,5%). Ocena ryzyka okołooperacyjnego według skali EuroSCORE II i STS również wykazywała u tych pacjentów najwyższą wartość, p<0,01.

W grupie chorych z zaawansowaną chorobą wieńcową omawianych w tej publikacji zgromadzono dodatkowo szczegółowe dane angiograficzne. Pacjenci zakwalifikowani do leczenia interwencyjnego – CABG lub PCI mieli średnio większą ilość zmian w naczyniach wieńcowych – 4,2±1,4 w kohorcie CABG i 4,3±1,5 w kohorcie PCI vs. 3,8±1,4 w grupie OMT, p<0,01 i częściej istotne (≥50%) zwężenie pnia lewej tętnicy wieńcowej (30,6% – CABG i 23,3% – PCI vs. OMT – 18,3%, p<0,01) niż grupa leczona zachowawczo. Podsumowując, chorzy zakwalifikowani przez kardiogrupę do postępowania zachowawczego jako jedynej formy leczenia byli najbardziej obciążeni klinicznie, jednak zaawansowanie choroby wieńcowej oceniane angiograficznie było największe w grupach strategii inwazyjnych. Całkowitą rewaskularyzację uzyskano u większego odsetka pacjentów w grupie CABG niż PCI (65,4% vs. 58,5%, p<0,01).

Wystąpienie pierwszorzędowego złożonego punktu końcowego zaobserwowano najczęściej u chorych w kohorcie OMT (154 (61,4%) pacjentów vs. 110 (30,9%) – kohorta CABG i 302 (44,5%) – kohorta PCI, p<0,01). Poza śmiertelnością wewnątrzszpitalną (która była najwyższa (ale nieistotnie statystycznie, p=0,68) w grupie OMT) oraz odsetkiem ponownej rewaskularyzacji wieńcowej (10,7% – CABG i 24,3% – PCI vs. 7,6% – OMT, p<0,01) strategie inwazyjne cechowały się mniejszą częstością występowania wszystkich pozostałych drugorzędowych punktów końcowych w porównaniu z kohortą OMT (p<0,01). Porównując jedynie leczenie interwencyjne – postępowanie kardiochirurgiczne było związane z mniejszym odsetkiem MACCE i ponownej rewaskularyzacji wieńcowej, podczas gdy pacjenci leczeni przezskórnie rzadziej doświadczyli udaru mózgu lub udaru mózgu zakończonego niepełnosprawnością (p<0,01). Jeśli chodzi o pozostałe drugorzędowe punkty końcowe, w leczeniu inwazyjnym nie zaobserwowano przewagi żadnej ze strategii.

Jakość życia chorych (oceniona z użyciem formularza SF-36) – zarówno komponenty: PCS, MCS, jak i całkowita nie różniły się w kohortach CABG, PCI i OMT podczas kwalifikacji kardiogrupy (p>0,05), natomiast na koniec okresu obserwacji chorzy leczeni kardiochirurgicznie ocenili swoją jakość życia – fizyczną, psychiczną i całkowitą jako najlepszą, podczas gdy w grupach PCI i OMT odnotowano odpowiednio gorsze i najgorsze wyniki (p<0,01).

W tej pracy wykazaliśmy, że w zaawansowanej chorobie wieńcowej wdrożenie przemyślanych strategii inwazyjnych starannie przedyskutowanych przez zespół kardiogrupy wydłuża życie, poprawia jego jakość oraz zmniejsza ryzyko groźnych powikłań.

W ostatniej publikacji z tego cyklu – artykule typu review przedstawiono – zgodnie z aktualną wiedzą medyczną – najobszerniejsze dostępne w literaturze zestawienie badań, doniesień i publikacji dotyczących funkcjonowania i wyników kwalifikacji kardiogrupy w kontekście pacjentów kardiologicznych – z chorobą wieńcową, zwężeniem zastawki aortalnej lub niedomykalnością zastawki mitralnej. W tej pracy podkreślono również istotę indywidualizacji podejścia Heart Teamu do każdego chorego, zaznaczając, że jest to klucz do sukcesu w leczeniu i poprawie jakości życia skomplikowanych klinicznie pacjentów obciążonych licznymi chorobami towarzyszącymi.

Przedstawiony cykl publikacji dotyczący wyników kwalifikacji kardiogrupy w warunkach referencyjnego ośrodka akademickiego wnosi do literatury przedmiotu szereg cennych nowości, które warto w tym miejscu wymienić. Przede wszystkim, grupa 1925 pacjentów z zaawansowaną chorobą wieńcową, zwężeniem zastawki aortalnej lub niedomykalnością zastawki mitralnej stanowi najliczniejszą w Polsce i jedną z najliczniejszych badanych prób wśród dostępnych w literaturze światowej artykułów i doniesień dotyczących tematyki kardiogrupy. Warto również podkreślić, że są to spójne dane pochodzące z jednego ośrodka kardiologicznego. Ponadto, okres obserwacji chorych jest wystarczająco długi, aby sformułować wnioski, które będzie można z korzyścią przełożyć na codzienną praktykę kliniczną. Wreszcie, innowacyjnością w przedstawionych publikacjach jest ocena jakości życia pacjentów, leczonych zgodnie z kwalifikacją kardiogrupy. Jest ona bezcenną wskazówką kliniczną dla specjalistów kardiogrupy, poprawiającą jakość podejmowanych w przyszłości decyzji, a według mojej najlepszej wiedzy dotychczas nieocenianą w literaturze tematu.

5. Heart Team – Results of Qualifications in Tertiary Cardiovascular Care Center [Summary]

The idea of Heart Team (HT) as a cooperation of experienced specialists making optimal therapeutic decisions for patients with multivessel coronary artery disease or valvular heart disease has an established position both in the European and American guidelines. A multidisciplinary approach, assessing clinical, angiographic and echocardiographic data, the risk of periprocedural complications, short- and long-term outcomes and patient preferences, seems to be the most rational tool deciding on the optimal management strategy for these "difficult" individuals, burdened with many comorbidities, often elderly, with cancer or frailty syndrome. At the 1st Department and Clinic of Cardiology of the Medical University of Warsaw, the tertiary cardiovascular care center, since 2016, meetings of cardiologists, cardiac surgeons, echocardiographists and specialists in many other fields of medicine are weekly held, aimed at presenting patients, communal discussion and selection of the optimal therapeutic method for further treatment. From 2016 to 2019, 176 HT meetings were held and a total number of 1,925 patients with multivessel coronary artery disease (MVD), aortic stenosis (AS) or mitral regurgitation (MR) were presented and then one of main three strategies: surgical, percutaneous or conservative was selected and implemented for each of them. Clinical, echocardiographic and angiographic data as well as the results of qualifications were collected retrospectively, and then patients were further follow-up to assess periprocedural complications, short- and long-term outcomes, as well as the quality of life depending on the implemented approach. Then, by plotting Kaplan-Meier curves for mortality and cardiovascular (CV) events in long-term follow-up for all main methods of treatment, statistical analysis was performed and the applied strategies were compared with each other.

In the first paper regarding the cooperation of HT at the 1st Department and Clinic of Cardiology, the clinical and echocardiographic characteristics, as well as the incidence of CV events and the quality of life of patients with severe symptomatic aortic stenosis (AS), qualified by HT specialists for one of the three main strategies: surgical aortic valve replacement (SAVR) with optimal medical therapy (OMT) – SAVR+OMT, transcatheter aortic valve replacement (TAVR) with optimal medical therapy – TAVR+OMT or only optimal medical therapy – OMT were evaluated.

From 2016 to 2019, during 176 HT meetings, 656 patients with AS were presented, and finally (after excluding individuals who did not meet the criteria of the study) 482 of them with severe symptomatic AS were included into final analysis. The patients were qualified and then treated according to HT

decisions as follows: SAVR+OMT – 85 patients, TAVR+OMT – 318 patients and OMT alone – 79 patients. The median follow-up was 866 days.

The patients qualified for the OMT strategy were the oldest (81.7±8.0 years) and presented with the most severe symptoms of HF (heart failure) [assessed using the NYHA (New York Heart Association) scale], p<0.01; nearly 75% of them were frailty, they were generally most burdened with comorbidities and with the highest risk of intervention, assessed both by the EuroSCORE II (European System for Cardiac Operative Risk Evaluation II) and STS (Society of Thoracic Surgeons) scales, p<0.01.

All patients were assessed by echocardiography – from the OMT–group at the time of HT discussion and from the SAVR– and TAVR–groups – before and after intervention (at the time of discharge from the hospital). Echocardiographic evaluation prior to the HT consultation showed statistically significant differences in the following parameters: LVEF (left ventricular ejection fraction) and the incidence of aortic bicuspid valve, which were the highest in the surgically-treated cohort (56.5±12.1% and 13 (15.3%), respectively, p <0.05) and the severity of AS assessed as aortic valve area indexed per square meter (m^2) of body surface area – AVAi (indexed aortic valve area), which was the lowest in the TAVR–group (0.45±0.16 cm^2/m^2, p<0.01). Postoperative evaluation showed a statistically significant improvement in echocardiographic parameters: LVEDD (left ventricular end-diastolic diameter), DVI (doppler velocity index) and pAVG (peak aortic valve gradient) in surgically–treated patients, p<0.01.

The incidence of the primary composite endpoint (death from any cause, non-fatal disabling stroke or non-fatal rehospitalization for AS) was significantly the highest in the OMT–group (94.9% vs. 32.9% and 34.6% for SAVR and TAVR, respectively, p<0.01). Moreover, the occurrence of secondary endpoints was statistically significantly less frequent in the SAVR– and TAVR–cohorts than in the conservatively–treated patients (p<0.05). Comparing only interventional strategies – TAVR–patients had lower rates of AKI (acute kidney injury), newly diagnosed AF (atrial fibrillation) and major bleeding (assessed as ≥ 3 according to the BARC scale (The Bleeding Academic Research Consortium)), p<0.05. Conversely, the superiority of SAVR for major vascular complications and need for PP (permanent pacemaker) implantation was noticed, p<0.05. However, no statistically significant differences between the SAVR– and TAVR–cohorts for primary and other secondary endpoints were observed. In-hospital mortality did not differ between interventional strategies (6 (7.1%) vs. 20 (6.3%) for SAVR and TAVR, respectively, p=0.80), while the length of stay in the intensive care unit was significantly prolonged in surgically–treated patients (4.2±3.7 days vs. 1.8±3.8 days for SAVR and TAVR, respectively, p<0.05).

The quality of life (assessed using the SF-36 questionnaire) – both the PCS (physical component summary), MCS (mental component summary) and total did not statistically differ at the time of HT consultations ($p>0.01$), while at the end of the follow-up, patients who were treated conservatively assessed their quality of life – PCS, MCS and overall much worse than those treated surgically or percutaneously ($p<0.01$). There were no statistically significant differences in the quality of life between patients who underwent SAVR or TAVR.

In this article, we showed that after careful qualification and accurate implementation of decisions made by experienced HT, invasive strategies provide better long-term outcomes and improve the quality of life of patients with severe symptomatic AS.

In the next paper, we outlined the clinical and echocardiographic characteristics, the results of HT qualifications as well as the long-term outcomes and quality of life of patients with severe symptomatic mitral regurgitation (MR), who were assessed by members of HT, and then treated according to their decisions with: surgical mitral valve replacement (MVR) with optimal medical therapy – MVR+OMT, transcatheter edge-to-edge repair (TEER) using the MitraClip (MC) system with OMT – MC+OMT or only conservatively – OMT.

From 2016 to 2019, during 176 HT meetings, 254 patients with MR were discussed, and ultimately (having inclusion and exclusion criteria) 157 individuals with severe symptomatic MR treated according to HT decisions (MVR+OMT – 46 patients, MC+OMT – 58 patients or OMT – 53 patients) were included into final analysis. The mean follow-up period (SD) was 29±15 months.

Regarding statistically significant differences in clinical characteristics, patients from the OMT–cohort were the oldest (73.7±11.05 years), had the highest coincidence of diabetes (64.2%), AF (41.5%) and COPD (chronic obstructive pulmonary disease) – 43.4%, $p<0.05$; among patients qualified for MVR, the highest percentage of primary MR (56.5%) and the lowest periprocedural risk assessed according to the EuroSCORE II scale were found, $p<0.05$, while patients from MC–group were the most frequently burdened with concomitant CKD (chronic kidney disease) – 94.8% and a history of previous CABG (coronary artery bypass grafting) – 29.3%; furthermore patients treated percutaneously had also the most severe symptoms of HF (assessed by NYHA scale), $p <0.05$.

For all patients with severe MR presented within HT meetings, we have provided full echocardiographic data. Summarizing, individuals qualified for MVR, MC or OMT differed significantly in following parameters: LVEF – the highest in the MVR–cohort (42.4±6.1%), LVEDD and ERO (effective regurgitation orifice area) – the lowest in the MVR–cohort (6.24±0.65 cm [centimeter] and 0.37±0.08 cm^2 [square centimeter], respectively) and mean MVG (mitral valve gradient) – the lowest in the MC–group (4.12±1.41 mmHg), $p<0.05$. The postoperative evaluation (after MVR or MC) showed significantly greater improvement in the percentage of degree of residual central regurgitation ≥ 2 and paravalvular leak and values of ERO, MR volume, maximum and mean MVG in the group of patients treated surgically as compared with MC ($p<0.05$).

In-hospital mortality did not differ significantly between the groups qualified for interventional strategies (4 (8.7%) vs. 1 (1.7%) for MVR and MC, respectively, $p=0.10$). The occurrence of the primary endpoint (death from CV cause) was the most frequent in the conservative cohort (20 (37.7%)), while in MVR and MC–groups – 7 (15.2%) and 10 (17.2%), respectively, $p=0.01$. Moreover, for the secondary endpoints (death from any cause, non-fatal MI (myocardial infarction), non-fatal stroke, non-fatal hospitalization for HF exacerbation, or total CV events), MVR and MC proved their superiority as compared with OMT strategy ($p<0.05$). The occurrence of primary and secondary endpoints did not significantly differ between interventional strategies (MVR and MC), $p>0.05$.

The quality of life (assessed using the SF-36 questionnaire) – both the PCS, MCS and total did not statistically differ at the time of HT qualifications ($p>0.05$), while at the end of the follow-up, patients from conservative group assessed their quality of life – PCS, MCS and overall as the worst ($p<0.01$).

In this study, we also demonstrated a significant role of the HT for management of patients with severe symptomatic MR – careful evaluation and subsequent implementation of decisions made by an experienced HT members resulted in better outcomes and improved quality of life of invasively–treated patients.

The last original paper composing the series presents the results of our internal HT consultations in patients with advanced CAD (coronary artery disease) [defined as 3-VD (three-vessel disease) and/or multivessel disease equivalent – LMS (left main stenosis; defined as ≥ 50% occlusion of left main artery)]; the clinical, echocardiographic and angiographic characteristics were outlined, and the incidence of complications, outcomes and the quality of life of participants were assessed.

From 2016 to 2019, 1509 patients with CAD were presented during 176 HT meetings, and ultimately (excluding patients who did not meet the criteria of the study) 1286 individuals with severe CAD (3-VD and/or LMS) were included in the final analysis. Patients were qualified according HT decisions for three main strategies as follows: surgical – CABG with OMT – CABG+OMT (356 patients), percutaneous – percutaneous coronary intervention (PCI) with OMT – PCI+OMT (679 patients) or conservative – OMT (251 patients). The primary composite endpoint was defined as MACCE (major adverse cardiac or cerebrovascular events) – death from any cause, MI, stroke or repeat revascularization. The above components considered separately, as well as composite of death from any cause, MI or stroke, CV death, in-hospital mortality, disabling stroke, and additionally – for interventional strategies: stent thrombosis or graft occlusion were defined as secondary endpoints. The mean follow-up (SD) for this group was 37±14 months.

Nearly 41% of the patients consulted during HT meetings were hospitalized with a diagnosis of ACS (acute coronary syndrome): STEMI (myocardial infarction with ST-segment elevation), NSTEMI (myocardial infarction without ST-segment elevation) or UA (unstable angina); 3.4% were in cardiogenic shock, and the rest had diagnosis of chronic coronary syndrome. Statistically significant differences in the clinical characteristics of patients were found – individuals qualified by HT only for conservative treatment were the oldest (72.5±9.9 years) and nearly 2/3 of them were frailty, $p<0.01$. Moreover, patients from the OMT–cohort most often: had the diagnosis of HF (92%) and presented with symptoms of severe symptomatic HF in class NYHA III-IV (51.4%), severe left ventricular systolic dysfunction – LVEF <30% (57%) and significantly increased LVEED (6.2±1.0 cm). Furthermore, they were most frequently burdened with AF (37.8%), CKD (76.9%), anemia (62.5%), severe PH (pulmonary hypertension) – 13.9% and a history of cancer (35.5%). Perioperative risk assessment according to EuroSCORE II and STS scales also showed the highest values in these patients, $p <0.01$.

For patients with severe CAD we also collected a detailed angiographic data, as each patient had coronary angiography. Summarizing, participants treated with CABG or PCI had greater number of affected coronary lesions (4.2±1.4 and 4.3±1.5 for CABG– and PCI–arm, respectively vs. 3.8±1.4 in the OMT-group, $p <0.01$) and more frequently LMS (30.6% and 23.3% for CABG and PCI, respectively vs. 18.3% in OMT–cohort, $p<0.01$). It is need to highlight that although the patients qualified by HT for conservative management as the only form of treatment were the most burdened clinically, the complexity of CAD assessed by angiography was the highest in patients qualified for invasive strategies. Complete revascularization was achieved in a greater percentage of patients in the CABG–group than in the PCI–arm (65.4% vs. 58.5%, $p<0.01$).

The occurrence of primary composite endpoint was most frequently observed in the OMT–cohort (154 (61.4%) patients vs. 110 (30.9%) and 302 (44.5%) in CABG and PCI, respectively, $p<0.01$). Excluding in-hospital mortality (which was the highest (but not statistically significant, $p=0.68$) in the OMT group) and repeat revascularization (10.7% and 24.3 % for CABG and PCI, respectively vs. 7.6% in OMT-patients, $p<0.01$), invasive strategies had a lower incidence of all other secondary endpoints as compared with conservative management ($p<0.01$). Comparing only interventional treatment, CABG was associated with a lower rates of MACCE and repeat revascularization, while patients treated with PCI experienced less strokes or disabling strokes ($p<0.01$). Regarding the remaining secondary endpoints, there was no advantage of any of interventional strategies.

Quality of life of patients (assessed using the SF-36 questionnaire) – both the PCS, MCS and total did not significantly differ in the CABG–, PCI– and OMT–cohorts within HT consultations ($p>0.05$), while at the end of the follow-up, patients treated surgically assessed their quality of life – physical, mental and total – as the highest, while in the PCI and OMT groups, respectively, worse and the worst results were obtained ($p <0.01$).

In this study, we showed that for individuals with severe CAD, the implementation of well-thought-out by HT and then carefully implemented invasive strategies prolongs life, improves its quality and reduces the risk of serious complications.

In the last article in the series – a state of art – the most comprehensive summary of studies, reports and publications available in the literature and regarding the HT issue in the context of cardiological patients (with CAD, AS or MR) was presented. This manuscript also highlights the importance of the individualized HT approach to each patient, emphasizing that it is the key to success in treatment and improving the quality of life of complex and highly burdened patients.

The presented series of articles regarding the results of HT qualifications in tertiary cardiovascular care center has several strengths that should be highlighted here. Firstly, the group of 1,925 patients with severe CAD, AS or MR is the most numerous in Poland and one of the most abundant among the articles and reports regarding HT issue that can be found in the literature; and it is worth emphasizing that these data come from only one cardiology center. Moreover, the follow-up is long enough to draw conclusions that can be usefully translated into real-life clinical practice. Finally, the innovation in the presented studies is the assessment of the quality of life of patients treated following HT decisions. It is a priceless clinical guideline for HT specialists, believed to improve the quality of decisions-making process in the future, and, to the best of my knowledge, so far assessed for the first time in the literature on this subject.

6. WSTĘP

6.1. Koncepcja kardiogrupy (Heart Team). Zarys problematyki.

Wraz ze starzejącą się populacją, zarówno polską, jak i europejską, możemy się spodziewać wzrostu częstości występowania miażdżycy, a na jej podłożu choroby wieńcowej i chorób zastawkowych serca – związanych z procesem zwyrodnieniowym lub o etiologii czynnościowej – wtórnej do remodelingu mięśnia sercowego, do którego dochodzi u chorych z niewydolnością serca. W środowisku lekarskim panuje niekwestionowane przekonanie, że standardy leczenia należy nieustannie poprawiać i możliwie najpełniej systematyzować z wykorzystaniem multidyscyplinarnych zespołów kardiologicznych (kardiogrupa, Heart Team), aby osiągnąć najbardziej satysfakcjonujące wyniki.

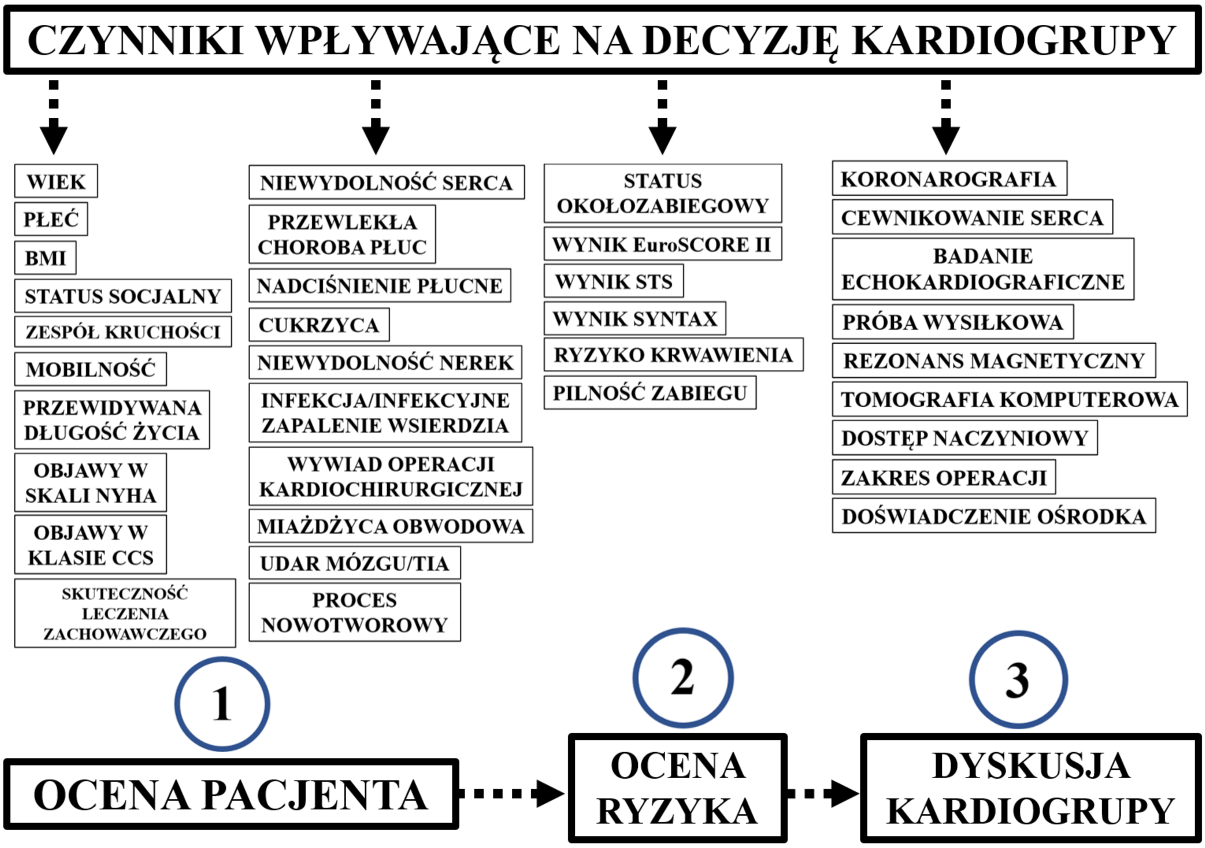
Zaangażowanie doświadczonego zespołu kardiologicznego jest najbardziej pożądane, zarówno przez lekarza, jak i pacjenta, aby starannie ocenić zalety i wady różnych strategii leczenia, a także sprostać oczekiwaniom chorych, nierzadko w podeszłym wielu, z wieloma chorobami współistniejącymi, zespołem kruchości lub ograniczoną sprawnością ruchową i psychiczną.

Mimo iż w aktualnych rekomendacjach zarówno europejskich, jak i amerykańskich towarzystw kardiologicznych znajdujemy zalecenia wskazujące jasno i dobitnie potrzebę inicjacji wielodyscyplinarnego zespołu i włączenia go w proces diagnostyczno-terapeutyczny u „skomplikowanych” chorych z wielonaczyniową chorobą wieńcową (MVD, multivessel disease) lub z zastawkową wadą serca (VHD, valvular heart disease) [1–7], rekomendacje te opierają się głównie na opiniach ekspertów, podczas gdy dowody z randomizowanych badań klinicznych (RCT, randomized-controlled trials) potwierdzających te zalecenia są nadal skąpe i często niejednoznaczne.

Kilka doniesień, które możemy znaleźć w literaturze przedmiotu sugeruje, że poprzez wspólne, zgodne z rekomendacjami, podejmowanie decyzji możliwa jest poprawa ogólnych wyników leczenia. Jest to jednak tylko przekonanie, ponieważ rzeczywiste dowody, którymi musimy się zadowolić, pochodzą z badań obserwacyjnych opisujących wyniki funkcjonowania i kwalifikacji kardiogrupy bez próby kontrolnej.

Wybór pomiędzy leczeniem interwencyjnym a zachowawczym w oparciu o wielodyscyplinarne podejmowanie decyzji pierwotnie wywodził się z koncepcji kardiogrupy, o której po raz pierwszy wspomniano w literaturze w późnych latach 70-tych XX wieku. [8, 9] Już wówczas podkreślono, że postępowanie dotyczące każdego „skomplikowanego” pacjenta powinno być omówione przez co najmniej trzech specjalistów – kardiologa „zachowawczego”, kardiologa interwencyjnego oraz kardiochirurga. Wraz z upływem lat i implementacją nowych metod leczenia struktury kardiogrupy zasilała coraz większa rzesza specjalistów, których aktywne uczestnictwo w konsultacjach Heart Teamu (HT) było zależne od złożoności przypadku.

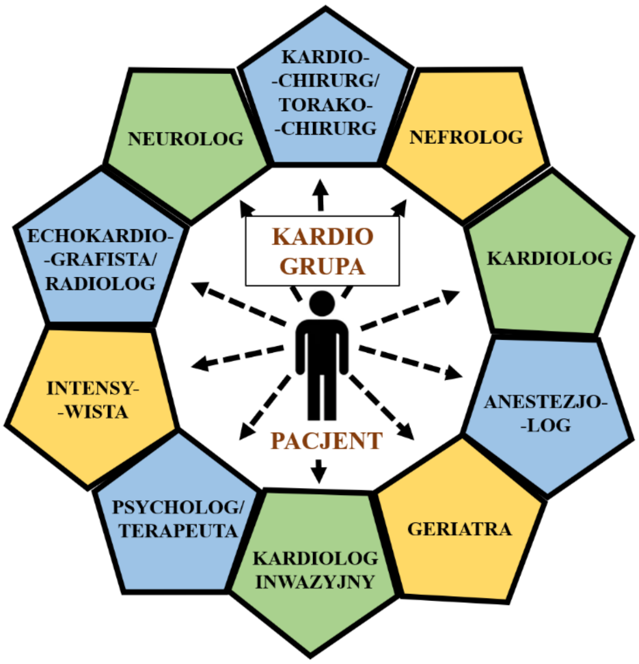
Ponadto, już wówczas, i również dziś istnieje wiele zmiennych parametrów związanych z procesem podejmowania decyzji, ponieważ działalność kardiogrupy powinna być w głównym stopniu skoncentrowana na pacjencie, a nie tylko na leczeniu wybranej jednostki chorobowej. Dlatego tak ważne w wielostopniowej kwalifikacji kardiogrupy jest podejście holistyczne, uwzględniające nie tylko ocenę kliniczną chorego, ale również możliwość dodatkowej ewaluacji, stratyfikację ryzyka, doświadczenie operatorów i warunki danego ośrodka (**Rycina 1**).



Rycina 1.

W obecnych czasach współpraca specjalistów kardiogrupy wydaje się praktycznie niemożliwa bez doświadczonego echokardiografisty, radiologa i innych specjalistów obrazowania, którzy mogą pomóc w określeniu zaawansowania choroby i zakresu planowanej interwencji oraz jej celowości i możliwościach wykonalności. Anestezjolog może pomóc w ocenie ryzyka okołozabiegowego u pacjenta, który ma zostać poddany operacji kardiochirurgicznej lub interwencji przezskórnej; ponadto określa bezpieczeństwo znieczulenia ogólnego. Specjalista intensywnej terapii jest zaangażowany w prowadzenie pacjenta w okresie pooperacyjnym. Wiedza i umiejętności nefrologa są bezcenne w sytuacjach, w których rozważana jest dializa lub w przypadku powikłań, takich jak ostre uszkodzenie nerek (AKI). Neurolog jest odpowiedzialny za ocenę ryzyka okołozabiegowych incydentów naczyniowo-mózgowych i może odroczyć planowany zabieg lub zalecić wcześniejszą interwencję w zakresie tętnic dogłowowych, jeśli uzna, że ich zwężenie lub niedrożność znacząco zwiększają możliwość komplikacji. Wreszcie, geriatra może być zaangażowany w ustalenie czy pacjent prezentuje cechy zespołu kruchości i ocenić celowość strategii interwencyjnej. Dowiedziono, że aspekt psychologiczny jest ważnym czynnikiem rozwoju chorób układu sercowo-naczyniowego, zatem psycholog lub psychoterapeuta powinni być również włączeni do procesu decyzyjnego.

Zarysowane powyżej wielodyscyplinarne podejście powinno być wymagane we wszystkich ośrodkach i aktywnie wdrażane przez zespół HT. Graficzną kooperację specjalistów kardiogrupy przedstawiono na **Rycinie 2**.



Rycina 2.

6.2. Wielonaczyniowa choroba wieńcowa – rola kardiogrupy.

Choroba wieńcowa (CAD, coronary artery disease) to zespół objawów klinicznych związanych z ograniczeniem lub całkowitym zablokowaniem przepływu krwi przez tętnice wieńcowe, najczęściej z powodu miażdżycy lub pęknięcia blaszki miażdżycowej i manifestujących się jako ostre lub przewlekłe zespoły wieńcowe. Tylko w 2019 roku na świecie odnotowano 197 milionów nowych przypadków choroby wieńcowej, co skutkowało śmiercią ponad 9 milionów ludzi. [10] Niezależnie od przebiegu klinicznego choroba wieńcowa jest jednym z najpoważniejszych problemów medycznych współczesnego świata, stąd zasadne wydaje się poszukiwanie nowych kierunków działania mogących wpłynąć na optymalizację jej diagnostyki, jak również zmniejszenie śmiertelności, zapobieganie niepełnosprawności oraz redukcję nakładów finansowych na leczenie.

Wraz z rosnącą liczbą metod leczenia przezskórnego i chirurgicznego, dostępnością nowych leków redukujących objawy dławicy i zmniejszających śmiertelność oraz zacieśnieniem współpracy między kardiologami i kardiochirurgami, idea kardiogrupy została wdrożona i nadal zajmuje centralną pozycję w opiece nad pacjentami z chorobą wieńcową (I klasa zaleceń w rekomendacjach europejskich i amerykańskich). [1 – 5] Podczas gdy podejmowanie decyzji u pacjentów w stanach ostrych, wymagających pilnej interwencji lub u chorych z mniej złożoną chorobą wieńcową może być jednomyślne, u stabilnych pacjentów z chorobą wielonaczyniową, HT składający się z kardiologa „zachowawczego", kardiologa interwencyjnego, kardiochirurga i echokardiografisty wydaje się być minimum w wyborze optymalnej metody rewaskularyzacji wieńcowej lub dyskwalifikacji z interwencji.

W oparciu o analizę danych dostępnych w literaturze podmiotu, poniżej podsumowano kluczowe doniesienia omawiające funkcjonowanie kardiogrupy u pacjentów z wielonaczyniową chorobą wieńcową.

W wieloośrodkowym, randomizowanym badaniu klinicznym Synergy Between PCI with Taxus and Cardiac Surgery (SYNTAX), w którym lokalny kardiolog interwencyjny i kardiochirurg oceniali prospektywnie pacjentów z wcześniej nieleczoną chorobą pnia lewej tętnicy wieńcowej (LM, left main) i/lub chorobą trójnaczyniową (3-VD, three-vessel disease) celem kwalifikacji do przezskórnej interwencji wieńcowej (PCI, percutaneous coronary intervention) lub pomostowania aortalno-wieńcowego (CABG, coronary artery bypass grafting), po raz pierwszy realnie wdrożono koncepcję kardiogrupy celem dalszej ewaluacji pacjentów z MVD. Częstość występowania poważnych niepożądanych zdarzeń sercowych lub naczyniowo-mózgowych (MACCE, major cardiac or cerebrovascular event) – zgon z jakiejkolwiek przyczyny, udar mózgu, zawał mięśnia sercowego (MI, myocardial infarction) lub powtórna rewaskularyzacja po 12 miesiącach follow-up'u była istotnie statystycznie wyższa w grupie leczonej przezskórnie (17,8% vs. 12,4% w kohorcie leczonej kardiochirurgicznie, p=0,002), głównie z powodu zwiększonego odsetka powtórnych rewaskularyzacji u pacjentów poddawanych PCI (13,5% vs. 5,9%, p<0,001). Odsetek zgonów i zawałów serca był podobny w grupach PCI i CABG, natomiast w grupie leczonej kardiochirurgicznie odnotowano większą częstość udarów mózgu. Jednakże w tym badaniu nie oceniano punktów końcowych u chorych zakwalifikowanych do leczenia zachowawczego, stąd fakt ten może być pewnym mankamentem, jeśli chodzi o pełną ocenę kwalifikacji kardiogrupy. [11]

W 2014 r. Head SJ., i in. przedstawili końcowe wyniki 5-letniego follow-up'u 1095 pacjentów z 3-VD z badania SYNTAX losowo zrandomizowanych do grupy CABG (n=549) lub PCI (n=546). Zgodnie z wynikami badania i konkluzją autorów postępowanie kardiochirurgiczne powinno pozostać standardem leczenia u chorych z 3-VD, ponieważ skutkowało istotnie niższymi wskaźnikami zgonów, zawałów serca i powtórnych rewaskularyzacji wieńcowych w porównaniu z chorymi leczonymi przezskórnie. Odsetek udarów był niezależny od wdrożonej strategii leczenia. [12]

W kolejnym badaniu – SYNTAX III Revolution zidentyfikowano tomografię komputerową (CT, computed tomography) jako nieinwazyjną alternatywę dla konwencjonalnej koronarografii. Badanie to nie skupiało się na randomizacji pacjentów i ocenie występowania punktów końcowych, ale randomizowało kardiologów i kardiochirurgów zrzeszonych w kardiogrupie celem podjęcia decyzji o optymalnej strategii leczniczej w zaawansowanej chorobie wieńcowej. Dwa niezależne, zaślepione wzajemnie, zespoły HT, składające się z kardiologa inwazyjnego, kardiochirurga i radiologa zostały zrandomizowane do oceny zaawansowania choroby wieńcowej u 223 pacjentów ze świeżo rozpoznaną chorobą LM lub 3–VD z wykorzystaniem angiotomografii (CTA, computed tomography angiography) lub konwencjonalnej koronarografii. Zgodność dwóch zespołów w ocenie kwalifikacji pacjentów do PCI lub CABG (pierwszorzędowy punkt końcowy) była bardzo wysoka – około 93%, podczas gdy współczynnik Kappa Cohena wyniósł 0,82, co wskazuje na prawie całkowitą zgodność obu niezależnych zespołów. [13]

Dodatkowa analiza przeprowadzona w badaniu SYNTAX III Revolution obejmowała ocenę komponenty czynnościowej, wykorzystującą ewaluację cząstkowej rezerwy przepływu wieńcowego (FFR, fractional flow reserve) uzyskaną z CTA naczyń wieńcowych (FFR_{CT}), co zdefiniowano jako drugorzędowy punkt końcowy. Wykazano, że ocena CTA naczyń wieńcowych z użyciem FFR_{CT} była wykonalna u 196 z 223 pacjentów z MVD (87,9%). Zastosowanie FFR_{CT} zmieniło kwalifikację kardiogrupy w 7% przypadków i w porównaniu z pojedynczą oceną CTA tętnic wieńcowych zmodyfikowało o 12% liczbę naczyń, w których możliwa była rewaskularyzacja. Ponadto zastosowanie FFR_{CT} zmniejszyło odsetek pacjentów z hemodynamicznie istotną chorobą trójnaczyniową z 92,3% do 78,8%, zmieniając ich kwalifikację z tercyli średniego i wysokiego wyniku SYNTAX do niskiego. [14]

Bardzo niedawno zastosowanie strategii SYNTAX II polegającej na uwzględnianiu zarówno parametrów klinicznych, jak i anatomicznych w kwalifikacjach kardiogrupy do rewaskularyzacji wieńcowej istotnie poprawiło wyniki leczenia w porównaniu z oceną SYNTAX, w której ewaluacji poddano wyłącznie anatomiczne zaawansowanie choroby wieńcowej. Do badania SYNTAX II włączono 454 pacjentów z noworozpoznaną chorobą trójnaczyniową i porównano ich z 315 i 334 chorymi ze zdefiniowanych we wcześniejszym badaniu SYNTAX kohort – odpowiednio PCI i CABG. Strategia SYNTAX II poprzez uwzględnienie oceny czynnościowej skutkowała mniejszą liczbą zwężeń poddawanych PCI, lepszą optymalizacją interwencji przezskórnych poprzez zastosowanie obrazowania wewnątrzwieńcowego (IVUS, intravascular ultrasound), a ponadto zwiększeniem odsetka rewaskularyzacji przewlekłych okluzji (CTO, chronic total occlusion) i optymalizacją terapii lekowej. Po 5 latach odsetek pacjentów, którzy doświadczyli poważnych zdarzeń sercowo-naczyniowych – MACCE (zgon z jakiejkolwiek przyczyny, udar mózgu, zawał serca lub rewaskularyzacja wieńcowa) wyniósł 21,5% w grupie SYNTAX II – i był istotnie niższy niż w kohorcie SYNTAX PCI (36,4%), $p<0,001$. Ponadto, wszystkie komponenty MACCE, z wyjątkiem udaru mózgu, występowały rzadziej w grupie PCI, leczonej z użyciem strategii SYNTAX II ($p<0,001$). Co więcej, również odsetek zakrzepicy w stencie po 5 latach był niższy wśród pacjentów stosujących strategię SYNTAX II (1,4% vs. 5,5% dla SYNTAX PCI, $p=0,004$). Wykazano podobną częstość MACCE w grupie SYNTAX II i kohorcie CABG SYNTAX I (21,5% vs. 24,6%, $p=0,35$). [15]

Również w kilku badaniach obserwacyjnych oceniano kwalifikacje kardiogrupy u pacjentów z chorobą wieńcową w warunkach jednoośrodkowych.

Bonzel T., i wsp. opisali długoterminowe wyniki leczenia u pacjentów z chorobą wieńcową zakwalifikowanych przez HT do PCI. Spośród 11 174 koronarografii, 3408 angiografii u pacjentów z de novo rozpoznaną chorobą wieńcową zostało przeanalizowanych przez specjalistów celem wyboru optymalnej metody postępowania, a następnie 1527 pacjentów, u których wykonano pierwszą w życiu PCI z powodu CAD zostało poddanych obserwacji. Autorzy konkludowali, że podejście multidyscyplinarne jest skutecznym narzędziem do podejmowania decyzji ad hoc i w trybie planowym oraz skutkuje długotrwałymi korzyściami klinicznymi. W okresie follow-up'u CABG wykonano u 15%, PCI u 37%, a koronarografię u 65% pacjentów; całkowita śmiertelność wyniosła 51%. Odsetek zgonów był podobny w chorobie jednonaczyniowej (1–VD, one-vessel disease) i u pacjentów dobranych pod względem wieku i płci, ale przeżywalność była istotnie zmniejszona u chorych z pierwszym w życiu PCI i rozpoznaniem choroby wielonaczyniowej. [16]

Abdulrahman M., i wsp. przedstawił bardzo interesujący związek pomiędzy hierarchią członków kardiogrupy, a wynikami konsultacji dla pacjentów z izolowaną chorobą wielonaczyniową. Decyzje dotyczące dalszych strategii leczenia: kardiochirurgicznego, przezskórnego lub zachowawczego podejmowano w przypadku 1) obecności kierownika oddziału kardiochirurgii (HOS, head of cardiovascular surgery) i ordynatora kardiologii (HOC, head of cardiology), 2) gdy dostępny był tylko jeden z nich lub 3) pod nieobecność zarówno HOS, jak i HOC. Gdy zarówno HOC, jak i HOS byli obecni, dostępny był tylko HOS lub tylko HOC, lub zarówno HOC, jak i HOS byli nieobecni, stosunek kwalifikacji CABG do PCI wynosił odpowiednio 3,35, 4,88, 1,17 i 2,23. Badanie to wykazało, że kwalifikacje HT są związane nie tylko z aktualnymi rekomendacjami, ale w dużym stopniu zależą od hierarchii wśród specjalistów kardiogrupy. [17]

W kolejnym badaniu oceniano przeżycie długoterminowe 366 pacjentów z chorobą wieńcową (74,1% z MVD, średnia wieku 69 ± 11 lat) konsultowanych podczas 51 spotkań kardiogrupy. W zależności od wyjściowej charakterystyki klinicznej i stratyfikacji ryzyka, pacjentów zakwalifikowano do CABG+OMT (n=102), PCI+OMT (n=127) lub tylko do OMT (n=137). Autorzy przeprowadzili wieloczynnikową analizę regresji w celu określenia zmiennych związanych ze strategią wybraną przez HT, która wykazała, że u pacjentów we wstrząsie kardiogennym lub z rozpoznaną chorobą trójnaczyniową (nie uwzględniając zwężenia LM [LMS, left main stenosis]) najczęściej decydowano o dalszym leczeniu przezskórnym (PCI+OMT), do CABG+OMT kwalifikowano chorych młodszych i z izolowanym LMS, natomiast do OMT – najstarszych i z cukrzycą. Przeżycie 3-letnie było równe odpowiednio 60,8%, 84,3% i 90,2% w kohortach OMT, PCI+OMT i CABG+OMT. Nie odnotowano istotnej statystycznie różnicy w przeżyciu pomiędzy kohortami ocenionymi, a następnie zakwalifikowanymi przez kardiogrupę do jednej ze strategii rewaskularyzacji: CABG+OMT lub PCI+OMT. [18]

W 2019 r. Dominiques CT., i in. przedstawili wyniki kwalifikacji kardiogrupy u blisko 1000 pacjentów z chorobą wieńcową – 69,4% chorych z chorobą jednonaczyniową i 30,6% chorych z MVD zakwalifikowanych po starannej ocenie HT do CABG, PCI, OMT lub dodatkowych metod diagnostycznych w zależności od liczby zwężonych tętnic wieńcowych, decyzji kardiogrupy i preferencji pacjentów. Mediana okresu obserwacji (IQR, interquartile range) wyniosła 4,6 (4,2–5,0) lat. Autorzy stwierdzili brak związku pomiędzy zwężeniem proksymalnego odcinka gałęzi przedniej zstępującej (LAD, left anterior descending), a zgonem z jakiejkolwiek przyczyny u pacjentów z jedno– lub dwunaczyniową chorobą wieńcową (16,4% vs. 15,7% u chorych bez zwężenia LAD, p=0,70), podczas gdy u pacjentów ze złożoną chorobą wieńcową ogólna śmiertelność była istotnie zwiększona w przypadku LMS z chorobą dwu– lub trójnaczyniową (26,9%), p=0,019. [19]

Young MN., i wsp. przedstawili prospektywnie oceniane wyniki kwalifikacji kardiogrupy u 166 pacjentów wysokiego ryzyka z chorobą wieńcową, których po dyskusji HT zakwalifikowano do CABG (n=49), PCI (n=79), OMT (n=34) lub terapii hybrydowej (n=1). Mediana (IQR) liczby lekarzy podczas posiedzenia kardiogrupy wynosiła 6 (5-8). Wraz ze wzrostem ryzyka okołooperacyjnego (niskie, pośrednie, wysokie) ocenionego z zastosowaniem skali STS-PROM (Society of Thoracic Surgeons Predicted Risk of Mortality) kardiochirurgicznie leczono rzadziej, a OMT zalecano coraz częściej, podczas gdy nie obserwowano podobnych trendów w decyzjach kardiogrupy dotyczących CABG, PCI lub OMT w zależności od zakwalifikowania względem skali SYNTAX. Wśród 129 pacjentów poddanych rewaskularyzacji wieńcowej (CABG lub PCI) śmiertelność wewnątrzszpitalna i 30-dniowa wyniosła odpowiednio 3,9% i 4,8%, podczas gdy odsetek 30-dniowych nieplanowanych rehospitalizacji wyniósł 16,4%, 22,4% i 17,6% odpowiednio dla PCI, CABG i OMT. [20]

W kolejnym badaniu porównywano wyniki kwalifikacji kardiogrupy i opóźnienie rewaskularyzacji u pacjentów z chorobą wielonaczyniową z 2 grup: ocenianej przez kardiogrupę (n=93) i grupy kontrolnej (n=93) porównywalnych pod względem klinicznym i angiograficznym. Nie odnotowano istotnych statystycznie różnic pomiędzy grupami w ryzyku sercowo-naczyniowym, dysfunkcji lewej komory serca, punktacji w skali STS i SYNTAX. Po dyskusji członków kardiogrupy odsetek pacjentów zakwalifikowanych do CABG wyniósł 63% i był istotnie wyższy niż w grupie kontrolnej (23%), $p<0,01$. Ewaluacja kardiogrupy doprowadziła do znacznego opóźnienia w leczeniu przezskórnym (PCI), podczas gdy nie miała wpływu na opóźnienie leczenia kardiochirurgicznego (CABG). [21]

Tsang MB., i wsp. przedstawili wyniki bardzo ciekawej analizy dotyczącej 234 pacjentów z chorobą wielonaczyniową, w której porównywano postępowanie wdrożone pierwotnie przez kardiologów interwencyjnych w latach 2012–2014 z zaleceniami specjalistów 8 zaślepionych kardiogrup w latach 2017–2018. Różnica w wyborze metody postępowania pomiędzy decyzjami kardiologów interwencyjnych, a wynikami konsultacji HT wystąpiła w prawie jednej trzeciej przypadków. Członkowie kardiogrupy wykazali statystycznie nieistotne, ale widoczne różnice w wyborze strategii leczenia w zależności od wykonywanej specjalizacji. Badacze nie odnotowali natomiast istotnych statystycznie różnic pomiędzy kardiologami interwencyjnymi a członkami kardiogrupy, jeśli chodzi o kwalifikację do CABG (p=0,62) lub PCI (p=0,15), podczas gdy leczenie zachowawcze było rzadziej zalecane przez kardiologa interwencyjnego niż przez kardiogrupę (p=0,04). [22]; i komentarz [23].

6.3. Zwężenie zastawki aortalnej – rola kardiogrupy.

Na przestrzeni lat obserwujemy poprawę poziomu opieki zdrowotnej i przewidujemy dalszy wzrost średniej długości życia, dlatego też ze względu na starzenie się społeczeństwa możemy się spodziewać, że częstość występowania zwyrodnieniowej dysfunkcji zastawki aortalnej będzie się zwiększać. Problem jest pilny, ponieważ zwężenie zastawki aortalnej (AS, aortic stenosis) jest najbardziej rozpowszechnioną chorobą zastawkową na świecie i nadal pozostaje najczęstszym wskazaniem do interwencji w obrębie zastawek serca w Europie i Ameryce Północnej [6,7]. Chirurgiczna wymiana zastawki aortalnej (SAVR, surgical aortic valve replacement) była pierwszym standardem leczenia pacjentów z AS, który redukował objawy kliniczne niewydolności serca i istotnie poprawiał rokowanie, natomiast od 2007 roku powszechnie dostępna jest mniej inwazyjna metoda leczenia – przezcewnikowa wymiana zastawki aortalnej (TAVR, transcatheter aortic valve replacement). Obecnie metody leczenia objawowego zwężenia lewego ujścia tętniczego obejmują zarówno chirurgię konwencjonalną, jak i leczenie przezskórne (TAVR) oraz zachowawcze – OMT, a ostateczny wybór strategii postępowania jest zależny od wielu zmiennych. Chociaż wiele badań randomizowanych (RCTs) porównywało wyniki leczenia kardiochirurgicznego i przezskórnego u pacjentów ze zwężeniem zastawki aortalnej, obciążonych wysokim, pośrednim i niskim ryzykiem, rola kwalifikacji kardiogrupy była w nich słabo podkreślona [24–30]. HT był narzędziem wykorzystywanym do wyjściowej oceny klinicznej chorych i stratyfikacji ryzyka okołooperacyjnego, ale zupełnie pomijanym przy wyborze optymalnego sposobu leczenia. Aktualne rekomendacje dotyczące interwencji u pacjentów ze zwężeniem zastawki aortalnej są oparte na wynikach badań randomizowanych i kompatybilne z kwalifikacjami kardiogrupy dla indywidualnych pacjentów (ponieważ większość z nich nie spełnia kryteriów włączenia do RCT) [6,7].

AS jest schorzeniem bardzo niejednorodnym i wybór najkorzystniejszej metody postępowania powinien być dokładnie przemyślany przez członków HT, z uwzględnieniem wieku, oczekiwanej długości życia, chorób współistniejących i zespołu kruchości, anatomii zastawki, trwałości bioprotezy zastawkowej, możliwości dostępu naczyniowego i lokalnego doświadczenia operatorów. Oczekując na randomizowane badanie kliniczne, oceniające skuteczność i wyniki długoterminowe kwalifikacji kardiogrupy, musimy się zadowolić wynikami pochodzącymi z badań obserwacyjnych.

Dubois C., i wsp. po raz pierwszy opisali prospektywne wyniki leczenia zwężenia zastawki aortalnej u 163 pacjentów wysokiego ryzyka, którzy po ocenie kardiogrupy zostali zakwalifikowani do przezcewnikowej implantacji zastawki aortalnej (TAVI, transcatheter aortic valve implantation) – 73 chorych, SAVR – 35 chorych lub OMT z przezskórną walwuloplastyką aortalną (PTAV, percutaneous transluminal aortic valvuloplasty) lub bez niej – 55 pacjentów. Autorzy raportowali, że TAVI i SAVR okazały się być istotnie statystycznie lepsze niż OMT/PTAV, jeśli chodzi o występowanie śmiertelności z jakiejkolwiek przyczyny lub zgonów sercowo – naczyniowych, natomiast nie wykazały swej wyższości w przypadku częstości powtórnych hospitalizacji sercowo-naczyniowych w ciągu jednego roku. Porównując podejście inwazyjne, złożony punkt końcowy oceniający bezpieczeństwo wdrożonej terapii (całkowita śmiertelność, udar mózgu, zagrażające życiu krwawienie, ostre uszkodzenie nerek, okołozabiegowy zawał serca, poważne powikłanie naczyniowe lub powtórna interwencja związana z dysfunkcją zastawkową) po 30 dniach faworyzował TAVI, podczas gdy ocena skuteczności (całkowita śmiertelność, ponowna hospitalizacja z przyczyn sercowo-naczyniowych, dysfunkcja zastawkowa) po roku wykazywała wyższość leczenia kardiochirurgicznego. [31]

Thyregod HGH., i in. raportowali bardzo złe rokowanie u pacjentów z ciężką AS zakwalifikowanych przez kardiogrupę do leczenia zachowawczego z istotnie niższą przeżywalnością w porównaniu z kohortami TAVI i SAVR, p<0,01. U 93 % pacjentów z ciężkim zwężeniem zastawki aortalnej specjaliści kardiogrupy zaproponowali leczenie interwencyjne, pomimo podeszłego wieku, nasilonych objawów i dużego obciążenia chorobami współistniejącymi, podczas gdy chorzy zakwalifikowani do postępowania zachowawczego byli starsi, z większą koincydencją przewlekłej obturacyjnej choroby płuc (COPD, chronic obstructive pulmonary disease), obwodowej miażdżycy (PAD, peripheral artery disease), przebytego zawału serca i choroby naczyń mózgowych. Pacjenci zakwalifikowani do leczenia zachowawczego mieli bardzo niekorzystne rokowanie i tylko 57 i 26% z nich przeżyło odpowiednio 1 i 3 lata [32].

Dane z ośrodka belgijskiego wykazały, że starannie przeprowadzona kwalifikacja do leczenia przezskórnego (TAVI) przekłada się na podobne wyniki i krótszy pobyt w szpitalu w porównaniu z leczeniem kardiochirurgicznym (SAVR), również u pacjentów o wysokim ryzyku. Bakelants E., i wsp. przedstawili kooperację HT w kontekście zdrowotno-ekonomicznym z ograniczoną dostępnością do procedur przezcewnikowych. Dla 405 prospektywnie włączonych pacjentów wysokiego ryzyka ze zwężeniem zastawki aortalnej zakwalifikowanych do SAVR – 98, TAVI – 188 lub OMT/PTAV – 116, TAVI i SAVR wykazały wyższość w stosunku do OMT/PTAV, jeśli chodzi o całkowitą śmiertelność lub zgon z przyczyn sercowo-naczyniowych w ciągu 1 roku, podczas gdy nie obserwowano różnic w odsetkach udarów mózgu/przemijających incydentów niedokrwiennych (TIA, transient ischemic attack) oraz rehospitalizacji z przyczyn sercowo-naczyniowych po 30 dniach i po 1 roku [33].

W retrospektywnym badaniu przeprowadzonym przez Rea CW. i wsp. oceniono wyniki leczenia 243 chorych z ciężką AS zakwalifikowanych przez kardiogrupę odpowiednio do SAVR – 26, TAVI – 200 lub OMT – 17. Pomiędzy leczonymi grupami nie obserwowano istotnych statystycznie różnic w wieku i ryzyku okołooperacyjnym ocenionym z użyciem skali EuroSCORE II (European System for Cardiac Operative Risk Evaluation). Przeżywalność po wykonaniu TAVI i SAVR była podobna (93% vs. 84% dla TAVI vs. SAVR po 1 roku i 85% vs. 84% dla TAVI vs. SAVR po 2 latach) i zbliżona do populacji ogólnej w tym samym wieku; natomiast istotnie statystycznie wyższa niż w grupie chorych zakwalifikowanych do OMT (73% i 54% odpowiednio po 1 i 2 latach, p = 0,002) [34].

W kolejnej pracy, wyniki leczenia 286 pacjentów wysokiego ryzyka ze zwężeniem zastawki aortalnej, zakwalifikowanych przez kardiogrupę do SAVR (n=53), TAVR (n=210) lub OMT (n=23) zostały ocenione prospektywnie z medianą follow-upu (IQR) trwająca 18 (11–26) miesięcy. Autorzy podkreślili wzrastającą na przełomie lat liczbę pacjentów ze zwężeniem zastawki aortalnej kierowanych do konsultacji HT. Śmiertelność wewnątrzszpitalna wyniosła 7,5% w przypadku SAVR (u 20% chorych w kohorcie SAVR dokonano jednoczasowo innej interwencji kardiochirurgicznej) i 3,4% w kohorcie TAVR, p=0,447. Całkowita śmiertelność w ciągu 1 roku i 2 lat nie różniła się istotnie pomiędzy grupami leczonymi kardiochirurgicznie i przezskórnie (14,0% vs.17,2% dla SAVR vs. TAVR po 1 roku i 17,2% vs. 25,9% dla SAVR vs. TAVR po 2 latach), podczas gdy pacjenci zakwalifikowani do OMT mieli najgorsze rokowanie – mniej niż 1/3 przeżyła rok [35].

6.4. Niedomykalność mitralna – rola kardiogrupy.

Dostępne badania oceniające rokowanie pacjentów z niedomykalnością mitralną (MR, mitral regurgitation) leczonych chirurgicznie, przezskórnie lub zachowawczo są nadal skromne i chociaż opublikowano wiele raportów podających przeżywalność tych chorych, tylko w nielicznych porównano wyniki leczenia inwazyjnego i zachowawczego.

Obecnie dostępne są tylko 2 randomizowane badania kliniczne (RCTs): EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) [37] oraz COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy) [38] podające wyniki leczenia zaawansowanej niedomykalności mitralnej. W badaniu EVEREST II 279 pacjentów z umiarkowanie ciężką lub ciężką niedomykalnością mitralną (stopień 3+ lub 4+) zostało losowo zrandomizowanych w stosunku 2:1 do 2 strategii leczenia – przezskórnej korekcji niedomykalności mitralnej z użyciem systemu MitraClip (MC) lub kardiochirurgicznej wymiany lub naprawy zastawki mitralnej (MVR, mitral valve replacement or repair). Mimo iż korekcja przezskórna była mniej skuteczna od konwencjonalnego leczenia kardiochirurgicznego jeśli chodzi o redukcję stopnia niedomykalności, a pacjenci z kohorty chirurgicznej uzyskali istotnie statystycznie lepsze wyniki po 12 miesiącach (pierwszorzędowy punkt końcowy – brak zgonu, operacji z powodu dysfunkcji zastawki mitralnej, lub niedomykalności w stopniu 3/4+) – 73% vs. 55% w grupie MC, p=0,007, obie grupy osiągnęły podobną poprawę kliniczną [37]. Po 5 latach odsetek złożonego punktu końcowego (brak zgonu, operacji z powodu niedomykalności mitralnej, lub niedomykalności w stopniu 3/4+) wynosił odpowiednio 44,2% i 64,3% w grupie MC i kohorcie chirurgicznej (p=0,01), jednakże odsetek śmiertelności nie faworyzował żadnej strategii (20,8% vs. 26,8% odpowiednio dla MC i MVR, p=0,4) [39].

W badaniu COAPT 610 pacjentów z niewydolnością serca (HF, heart failure) i umiarkowanie ciężką (3+) lub ciężką (4+) wtórną niedomykalnością mitralną, u których utrzymywały się objawy niewydolności serca, pomimo zastosowania maksymalnie tolerowanej terapii zachowawczej, zostali losowo przydzieleni w stosunku 1:1 do MC+OMT lub OMT. Po 24 miesiącach follow-up'u leczenie przezskórne (MC) w porównaniu z zachowawczym wiązało się z istotnie statystycznie lepszymi wynikami: rocznym odsetkiem hospitalizacji z powodu HF (odpowiednio 35,8% vs. 67,9% dla MC vs. OMT, p<0,001) i ogólną śmiertelnością (odpowiednio 29,1% vs. 46,1% dla MC vs. OMT, p<0,001). Odsetek braku powikłań związanych z implantowanym urządzeniem po 12 miesiącach był bardzo wysoki – 96,6%. [38]

Jednakże w przedstawionych RCTs udział HT w podejmowaniu optymalnych decyzji terapeutycznych u pacjentów z objawową niedomykalnością mitralną nie został szczegółowo opisany. Mimo iż rola kardiogrupy została podkreślona w aktualnych rekomendacjach dotyczących wad zastawkowych serca [6,7], pozycja HT w leczeniu pacjentów z niedomykalnością mitralną opiera się wyłącznie na opiniach ekspertów i wynikach kilku badań obserwacyjnych.

Heuts S., i wsp. przedstawili wyniki badania jednoośrodkowego, w którym 158 pacjentów z MR zostało zakwalifikowanych przez HT do różnych strategii leczenia – chirurgicznej izolowanej lub jednoczasowej wymiany zastawki mitralnej (MVR) – 67 pacjentów, interwencji przezcewnikowej (przezskórnej korekcji z zastosowaniem MC lub naprawy zastawki mitralnej) – 20 pacjentów lub zachowawczej (71 pacjentów). 30-dniowa śmiertelność wyniosła 3 (4,4%), 0 (0,0%) i 3 (4,2%) odpowiednio dla MVR, leczenia przezskórnego i zachowawczego. Z użyciem narzędzi analizy statystycznej z medianą obserwacji 450 dni wykazano poprawę przeżycia chorych leczonych operacyjnie [40].

W innym badaniu Külling M., i wsp. przedstawili wyniki konsultacji 400 pacjentów z niedomykalnością mitralną, zakwalifikowanych zgodnie z decyzją kardiogrupy do następujących metod leczenia – MC (179 pacjentów), chirurgicznej naprawy zastawki mitralnej – 185 pacjentów lub MVR – 36 pacjentów. Wyniki leczenia ze średnim (SD) okresem obserwacji wynoszącym 32,2 (17,6) miesiąca były najlepsze dla chorych poddanych chirurgicznej naprawie zastawki mitralnej – mieli oni wyższy 4-letni okres przeżycia (HR 0,40; 95% CI 0,26 do 0,63; p<0,001) i niższy odsetek złożonego punktu końcowego (zgon z jakiejkolwiek przyczyny, ponowna hospitalizacja z powodów sercowo-naczyniowych lub ponowna interwencja w zakresie zastawki mitralnej) w porównaniu z kohortami MVR i MC [41].

Bardzo niedawno Nia PS., i wsp. podali, że dedykowany mitralny HT może zapewnić lepsze wyniki kwalifikacji pacjentów z chorobą zastawki mitralnej. Łączna liczba 1145 chorych – 641 ocenianych przez dedykowany mitralny HT i 504 przez ‘zwykły’ HT zostało włączonych do analizy. Po 1 roku śmiertelność była równa odpowiednio: 74 (14,7%) w grupie HT i 57 (8,9%) dla dedykowanej mitralnej kardiogrupy (p=0,002). Po 5 latach prawdopodobieństwo przeżycia zostało oszacowane jako 0,74 dla dedykowanej mitralnej kardiogrupy w porównaniu z 0,70 w grupie HT (p=0,04). Ograniczeniem tego badania może być jego nierandomizowany charakter; jednak w tym przypadku tego rodzaju podejście wydaje się nie być konieczne, gdyż intuicyjnie oczywiste jest, że dedykowany zespół zapewnia lepsze wyniki niż zespół ogólny. [42]

6.5. Uzasadnienie połączenia prac w cykl publikacji.

Prace wchodzące w skład cyklu tworzą spójną całość, naświetlając ważny aspekt wielodyscyplinarnego współdziałania specjalistów kardiogrupy w podejmowaniu trudnych decyzji terapeutycznych u pacjentów z wielonaczyniową chorobą wieńcową lub zastawkową wadą serca. Szczegółowe przedstawienie charakterystyki chorych oraz długoterminowych wyników kwalifikacji w perspektywie referencyjnego ośrodka akademickiego stanowi cenną wiedzę kliniczną, potwierdzającą obecne rekomendacje europejskich i amerykańskich towarzystw kardiologicznych. W artykule review przedstawiono i skomentowano najobszerniejszą dostępną wiedzę dotyczącą aktualnej pozycji kardiogrupy w chorobie wieńcowej, zwężeniu zastawki aortalnej i niedomykalności zastawki mitralnej, nawiązując również do cyklu prezentowanych publikacji.

7. CELE PRACY

Celem przedstawionej pracy doktorskiej było przedstawienie wyników kwalifikacji kardiogrupy u pacjentów z chorobą wieńcową, zwężeniem zastawki aortalnej lub niedomykalnością zastawki mitralnej w perspektywie referencyjnego ośrodka akademickiego, a w szczególności:

1. Prezentacja charakterystyki klinicznej, echokardiograficznej i angiograficznej pacjentów oraz wyników kwalifikacji kardiogrupy w referencyjnym ośrodku akademickim.
2. Przedstawienie powikłań okołozabiegowych oraz krótkoterminowych i odległych wyników leczenia pacjentów zgodnie z kwalifikacją kardiogrupy.
3. Omówienie aktualnego stanu wiedzy dotyczącego kardiogrupy w świetle aktualnych rekomendacji towarzystw europejskich i amerykańskich.

8. PRACE TWORZĄCE CYKL PUBLIKACJI

Rozdziały 8.1. – 8.4. stanowią cykl oryginalnych publikacji wchodzących w skład prezentowanej rozprawy doktorskiej.

8.1. Heart Team for Optimal Management of Patients with Severe Aortic Stenosis—Long-Term Outcomes and Quality of Life from Tertiary Cardiovascular Care Center.

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Clinical Medicine

Article

Heart Team for Optimal Management of Patients with Severe Aortic Stenosis—Long-Term Outcomes and Quality of Life from Tertiary Cardiovascular Care Center

Szymon Jonik [1], Michał Marchel [1,*], Ewa Pędzich-Placha [1], Zenon Huczek [1], Janusz Kochman [1], Piotr Ścisło [1], Paweł Czub [2], Radosław Wilimski [2], Piotr Hendzel [2], Grzegorz Opolski [1], Marcin Grabowski [1] and Tomasz Mazurek [1,†]

1 1st Department of Cardiology, Medical University of Warsaw, Banacha 1a Str., 01-267 Warsaw, Poland; szymonjonik.wum@gmail.com (S.J.); ewa.pedzich@wp.pl (E.P.-P.); zhuczek@wp.pl (Z.H.); j.kochman@tlen.pl (J.K.); piotr.scislo@wum.edu.pl (P.Ś.); grzegorz.opolski@wum.edu.pl (G.O.); marcin.grabowski@wum.edu.pl (M.G.); tomasz.mazurek.wum@gmail.com (T.M.)

2 Department of Cardiac Surgery, Medical University of Warsaw, Banacha 1a Str., 01-267 Warsaw, Poland; pczub@wum.edu.pl (P.C.); radoslaw.wilimski@wum.edu.pl (R.W.); phendzel@wum.edu.pl (P.H.)

* Correspondence: michal.marchel@wum.edu.pl; Tel.: +48-22-599-19-58; Fax: +48-22-599-19-57

† Senior author.

Abstract: Background: This retrospective study was proposed to investigate outcomes of patients with severe aortic stenosis (AS) after implementation of various treatment strategies following dedicated Heart Team (HT) decisions. Methods: Primary and secondary endpoints and quality of life during a median follow-up of 866 days of patients with severe AS qualified after HT discussion to: optimal medical treatment (OMT) alone, OMT and transcather aortic valve replacement (TAVR) or OMT and surgical aortic valve replacement (SAVR) were evaluated. As the primary endpoint composite of all-cause mortality, non-fatal disabling strokes and non-fatal rehospitalizations for AS were considered, while other clinical outcomes were determined as secondary endpoints. Results: From 2016 to 2019, 176 HT meetings were held, and a total of 482 participants with severe AS and completely implemented HT decisions (OMT, TAVR and SAVR for 79, 318 and 85, respectively) were included in the final analysis. SAVR and TAVR were found to be superior to OMT for primary and all secondary endpoints ($p < 0.05$). Comparing interventional strategies only, TAVR was associated with reduced risk of acute kidney injury, new onset of atrial fibrillation and major bleeding, while the superiority of SAVR for major vascular complications and need for permanent pacemaker implantation was observed ($p < 0.05$). The quality of life assessed at the end of follow-up was significantly better for patients who underwent TAVR or SAVR than in OMT-group ($p < 0.05$). Conclusions: We demonstrated that after careful implementation of HT decisions interventional strategies compared to OMT only provide superior outcomes and quality of life for patients with AS.

Keywords: heart team; aortic stenosis; heart failure; transcatheter aortic valve replacement; surgical aortic valve replacement; optimal medical therapy

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1. Introduction

Aortic valve stenosis (AS) is the most widespread valvular heart disease (VHD) in the world and still remains the most common primary cause for valve surgery or catheter intervention in Europe and North America [1,2]. The increase in incidence of degenerative senile AS due to ageing of the population is expected. The prevalence of AS is relatively low among young and middle-aged (in the absence of a congenital abnormality), while its general presence is about 5% of the population at age of 65 years and 12.4% of elderly, affected 3.4% of severe AS in those aged 75 years and older, with this note, if patients with severe, symptomatic AS left untreated, have a limited life expectancy [3]. With a growing number of therapeutic options, an idea of multidisciplinary heart team (HT) for the management of individuals with complex diseases has been implemented and now plays a central concept in the care of patients with AS (class I recommendation) [1,2]. An approach of multidisciplinary experienced team, taking into account clinical, angiographic and echocardiographic data, risk stratification, long-term prognosis and patients preferences seems to be a rational tool, deciding on the best treatment method for these patients, burdened with many co-morbidities. The options for treating of severe symptomatic AS include surgical aortic valve replacement (SAVR)—the unique and undisputable reference procedure for many years, transcatheter aortic valve replacement (TAVR)—less invasive, but increasingly used for inoperable or prohibitive risk for surgery and optimal medical therapy (OMT) as a palliative care. As recommended by specialists in European and American guidelines for VHD, for all patients qualified for interventional treatment, the final decision between SAVR versus (vs.) TAVR should be considered by the HT after careful comprehensive evaluation of given individuals, favoring TAVR in elderly patients who are inoperable or at increased risk for surgery [1,2]. However, while the idea of HT is generally adopted in the medical society, no clear consensus on how HT should cooperate and what the desired goals are is established; most importantly, long-term results of HT decisions implementation and patients satisfaction are still poorly investigated. To our knowledge, some research papers regarding the influence of HT decisions on prognosis of AS-patients are available in the literature [4–16]; however, there are still few studies describing real-life HT cooperation, and more evidence investigating HT consistency and significance of decision making and performance on hard clinical endpoints are required. The purpose of this study is to evaluate AS-patients management, long-term outcomes and quality of life following HT decisions implementation in the daily clinical practice of a tertiary cardiovascular care center. We believe that the obtained results and conclusions we excogitated will be supportive for emphasizing the evidence-based role of HT in the decisions-making process for VHD-patients.

2. Methods and Study Design

This single-center cohort study was conducted in the 1st Department of Cardiology, Medical University of Warsaw, a large tertiary cardiovascular care center in Poland. A total number of 656 patients that consulted for severe symptomatic AS during 176 HT meetings in 2016–2019 were enrolled in the retrospective analysis. The inclusion criteria were: aged ≥18 years and complete clinical, echocardiographic and angiographic characteristics. The exclusion criteria included the following: pregnancy/lactation, disseminated neoplastic process and life expectancy <1 year. All of patients were evaluated in a weekly meeting by a HT composed of interventional cardiologists, cardiac surgeons, clinical cardiologists and non-invasive imaging specialists and qualified after HT discussion to one of three main strategies: OMT alone, OMT and TAVR or OMT and SAVR. Sequentially, 131 (20.0%) patients were excluded from further analysis due to: not meeting severe AS criteria, qualification for combined surgery—SAVR + mitral valve surgery or/and CABG (coronary artery bypass grafting), valve-in-valve intervention or active endocarditis—69, 43, 10, and 9 patients, respectively. The severe AS for all symptomatic patients in our study was defined as aortic valve area [AVA] < 1.0 cm^2 (square centimeter) accompanying with aortic valve area indexed to BSA (body surface area) [AVA I] < 0.6 cm^2/m^2 (square centimeter per square meter), peak aortic-jet velocity (PAV) ≥ 4.0 m/s (meter per second) and mean aortic valve gradient (AVG) ≥ 40 mm Hg assessed by echocardiography (in accordance to ESC guidelines) [1]. Out of the 525 (80.0%) patients (54 (10.3%) cases re-discussed) that qualified for OMT, TAVR or SAVR, a total number of 43 (8.2%) participants were excluded due to: no consent with patient preference, loss of follow-up or death before implementation—21, 13, and 9 patients, respectively. Ultimately, in the final study, 482 (73.5%) patients with completely implemented HT decisions (OMT, TAVR, SAVR—79, 318, 85 patients, respectively) were included. OMT was defined as use of drugs as angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), angiotensin receptor-neprilysin inhibitors (ARNI), beta-blockers, digoxin, loop diuretics agents and aldosterone antagonists (MRA) in a manner that provides optimal reduction of the signs and symptoms of heart failure (HF) associated with aortic valve defect. The severity of HF symptoms was assessed using New York Heart Association (NYHA) classification, chronic kidney disease (CKD) defined as glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2 (millilitres per minute per 1.73 square meter), severe pulmonary arterial hypertension (PAH) as pulmonary artery systolic pressure (PASP) > 55 mmHg, anemia as hemoglobin level < 12 g/dL for women and <14 g/dL for men (g/dL—gram/decilitre), cancer—as active or up to 5 years back and smoking—as active or in the past. As the primary endpoint composite of all-cause mortality, non-fatal disabling strokes and non-fatal rehospitalizations due to AS at the end of follow-up (EOF) was considered, while assessed independently: the above three separately, cardiovascular (CV) death, non-fatal myocardial infarctions (MI), non-fatal strokes (disabling and non-disabling) for all strategies and new onset of atrial fibrillation (AF), acute kidney injury (AKI), infective valve endocarditis, need for permanent pacemaker implantation (PPI), major bleeding assessed by BARC (The Bleeding Academic Research Consortium) $\geq$ 3, major vascular complications and aortic valve re-interventions for TAVR and SAVR were only determined as secondary endpoints. All participants were observed for occurrence of endpoints with median follow-up of 866 (maximum—1824; minimum—365) days. The main outline of the study was presented in Figure 1. Additionally, general health status, using the short-form (SF)-36 questionnaire (totally and separately for physical component summary (PCS) and mental component summary (MCS)) before SAVR, TAVR and HT discussion (for patients qualified for OMT) and at the EOF for all alive participants (31 December 2020) was assessed. We have not yet obtained ethical/institutional review board (IRB) approval for our research, however, due to observational nature of the study, in accordance with applicable regulations, it is not required.

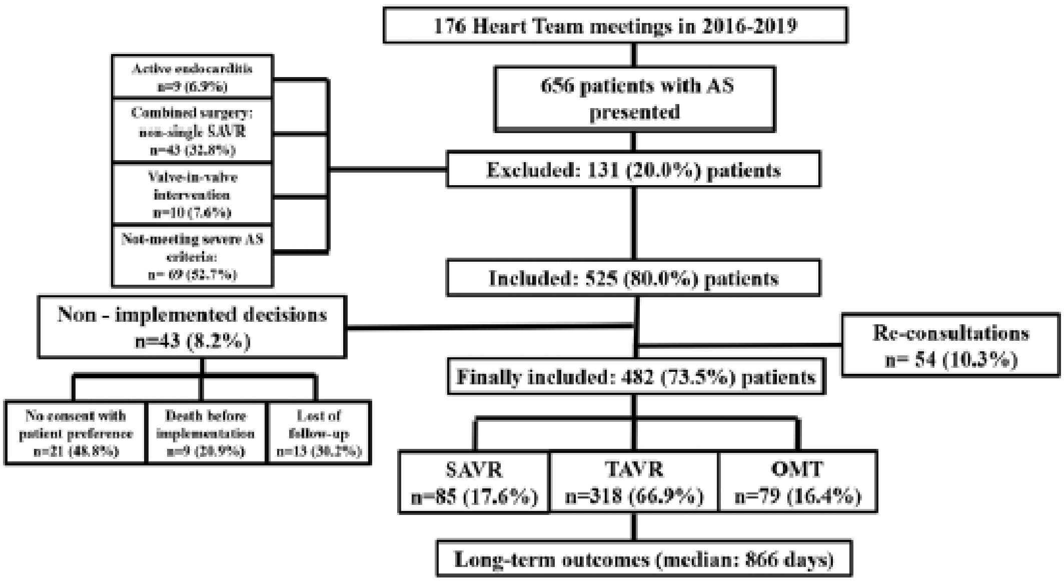

Figure 1. Study design. AS—aortic stenosis; TAVR—transcatheter aortic valve replacement; SAVR—surgical aortic valve replacement; OMT—optimal medical therapy.

Statistical Analysis

The PQStat software (version 1.6.6, PQStat, Poznań, Poland) was used for statistical analysis. The normality of distribution for continuous variables was confirmed with the Shapiro–Wilk test. Categorical data were expressed as counts and percentages, while continuous data were presented as mean ± SD. The comparison between groups of patients qualified for individual treatment strategies was performed using chi-square test and the statistical analysis was executed using 1-way analysis of variance (ANOVA). To compare the outcomes for all strategies with each other the hazard ratios (HRs) with 95% confidence intervals (95% CI) were calculated. To determine the independent predictors of outcomes in long term follow-up depending on the implemented HT-treatment strategy, multivariable, and multinominal logistic regression models were generated. Time to event analysis was performed using Kaplan–Meier curves. All *p* values (*p*) were given as least 2-sided, and *p* values lower than 0.05 were considered statistically significant.

3. Results

3.1. Study Population

From January 2016 to December 2019, 176 HT meetings were held, and a total of 482 patients with severe symptomatic AS meeting inclusion and exclusion criteria with completely implemented HT decisions (225 (46.7%) male, age (years, mean (SD)) = 78.1 (7.9), BMI [Body Mass Index] (kg/m^2 [kilogram per square meter], mean (SD)) = 27.8 (4.9), 400 (83.0%) with symptoms of HF, NYHA (class, mean (SD)) = 2.35 (0.79), EuroSCORE II [European System for Cardiac Operative Risk Evaluation II] (%, mean (SD)) = 9.3 (9.7), STS score [Society of Thoracic Surgeons score] (%, mean (SD)) = 5.9 (2.0) and given co-morbidities) were followed up. The average delay from HT decision to implementation was (min–max): 39 (2–171) and 27 (2–58) days for TAVR and SAVR, respectively, $p = 0.001$. As regards statistically significant differences between TAVR, SAVR and OMT groups, patients qualified for OMT were older, more often frail, presented more often with HF, CAD, history of previous MI and percutaneous coronary intervention (PCI), stroke, peripheral artery disease (PAD), anemia, chronic pulmonary obstructive disease (COPD), cancer, more symptomatic (according to NYHA), with severe PH and more than moderate mitral regurgitation (MR) and tricuspid regurgitation (TR) assessed by echocardiography and with the highest risk of intervention assessed both by EuroSCORE II and STS score than those with implemented TAVR or SAVR, those qualified for TAVR had the highest BMI, were more often burdened with atrial fibrillation (AF), CAD and with history of pacemaker implantation ($p < 0.05$ for all). Baseline clinical characteristics (overall and by groups) in details was presented in Table 1.

3.2. Echocardiographic Parameters

All patients were assessed by echocardiography—from the OMT-group at the time of HT discussion and from the SAVR- and TAVR-groups before and after intervention (at the time of discharge from the hospital). Statistically significant differences in echocardiographic parameters before HT decisions implementation were observed in the following: ejection fraction of left ventricle (LVEF) and incidence of bicuspid valve with the highest in the SAVR-group and evaluation of severity of aortic stenosis assessed by AVA I with the lowest in the SAVR-group ($p < 0.05$ for all). The results of echocardiographic parameters of prosthetic valve assessed after SAVR or TAVR implementation differ between these two groups for LVEDD, Doppler velocity index (DVI) and peak AVG and were significantly better for SAVR-patients ($p < 0.05$ for all). The detailed echocardiographic results before and after implementing HT decisions were collected in Table 2.

3.3. Endpoints

The occurrence of the primary endpoint was statistically most frequent in OMT-group (75 patients (94.9%)), comparing to the SAVR and TAVR groups—28 (32.9%) and 110 (34.6%) patients, respectively ($p < 0.05$). Additionally, SAVR and TAVR were found to be significantly superior to OMT for all secondary endpoints ($p < 0.05$). Considering the endpoints for interventional strategies only—TAVR was associated with reduced risk of AKI (30 days), new onset AF (30 days and at the EOF) and major bleeding >3 according to BARC (30 days and at the EOF)—$p < 0.05$ for all. Conversely, the superiority of SAVR for major vascular complications (30 days) and need for PPI (30 days and at the EOF) was observed ($p < 0.05$ for all). However, no statistically significant differences between SAVR and TAVR for primary endpoint and other secondary endpoints were noticed. In-hospital mortality did not statistically differ between SAVR and TAVR strategy (6 (7.1%) vs. 20 (6.3%); $p = 0.80$), while length of stay (days (SD)) in the intensive care unit (ICU) was significantly longer for SAVR-patients (4.25 (3.7) vs. 1.83 (3.8); $p < 0.05$). The endpoints comparing TAVR, SAVR and OMT were detailed in Table 3. We also performed a subanalysis of patients with active or previous cancer qualified after HT evaluation to TAVR, SAVR or OMT. From the entire population of these individuals ($n = 69$; 14.3%), patients qualified for OMT had a significantly increased risk of all-cause mortality as compared with the TAVR and SAVR-groups ($p < 0.01$), while no differences in other outcomes were observed. Evaluating this subgroup for interventional strategies only, the higher incidence of major bleeding (EOF) in TAVR-patients vs. the SAVR-cohort was demonstrated ($p < 0.01$), while other endpoints did not differ significantly. The Kaplan–Meier curves comparing all strategies for primary and secondary endpoints were presented in Figure 2.

Table 1. Baseline clinical characteristics.

Baseline Characteristic	Overall (482)	TAVR (318)	SAVR (85)	OMT (79)	*p* Value
Age, years; mean (SD)	78.1 (7.9)	79.0 (7.2)	71.0 (6.2)	81.7 (8.0)	<0.01
Gender, male (%)	225 (46.7)	149 (46.9)	44 (51.8)	32 (40.5)	0.35
BMI, kg/m^2; mean (SD)	27.8 (4.9)	28.2 (4.8)	27.9 (3.9)	26.4 (5.9)	0.01
Heart Failure, *n* (%)	400 (83.0)	279 (87.7)	50 (58.8)	71 (89.9)	<0.01
NYHA, mean (SD)	2.35 (0.79)	2.28 (0.71)	2.17 (0.77)	2.84 (0.93)	<0.01
CAD, *n* (%)	284 (58.9)	188 (51.9)	39 (45.9)	57 (72.2)	<0.01
Diabetes, *n* (%)	176 (36.5)	120 (37.7)	23 (27.1)	33 (41.8)	0.11
Hypertension, *n* (%)	417 (86.5)	276 (86.8)	72 (84.7)	69 (87.3)	0.86
Previous stroke/TIA, *n* (%)	47 (9.8)	30 (9.4)	4 (4.7)	13 (16.5)	0.04
Atrial fibrillation, *n* (%)	171 (35.5)	122 (38.4)	19 (22.4)	30 (38.0)	0.02
Previous MI, *n* (%)	99 (20.5)	49 (15.4)	13 (15.3)	37 (46.8)	<0.01
Previous PCI, *n* (%)	246 (51.0)	167 (52.5)	30 (35.3)	49 (62.0)	<0.01
Previous CABG, *n* (%)	53 (11.0)	29 (9.1)	10 (11.8)	14 (17.7)	0.09
Previous non-aortic VS, *n* (%)	25 (5.2)	14 (4.4)	3 (3.5)	8 (10.1)	0.09
History of pacemaker, *n* (%)	71 (14.7)	57 (17.9)	1 (1.2)	13 (16.5)	<0.01
≥Moderate MR, *n* (%)	26 (5.4)	11 (3.5)	3 (3.5)	12 (15.2)	<0.01
≥Moderate TR, *n* (%)	26 (5.4)	14 (4.4)	1 (1.2)	11 (13.9)	<0.01
PAD, *n* (%)	86 (17.8)	48 (15.1)	9 (10.6)	29 (36.7)	<0.01
CKD, *n* (%)	303 (62.9)	223 (70.1)	31 (36.5)	49 (62.0)	<0.01
Anemia, *n* (%)	289 (60.0)	206 (64.8)	25 (29.4)	58 (73.4)	<0.01
Dyslipidemia, *n* (%)	371 (77.0)	248 (78.0)	64 (75.2)	59 (74.7)	0.76
COPD, *n* (%)	72 (14.9)	42 (13.2)	6 (7.1)	24 (30.4)	<0.01
Severe PH, *n* (%)	46 (9.5)	21 (6.6)	3 (3.5)	22 (27.8)	<0.01
Cancer, *n* (%)	69 (14.3)	39 (12.3)	9 (10.6)	21 (26.6)	<0.01
Smoking, *n* (%)	323 (67.0)	216 (67.9)	53 (62.4)	54 (68.4)	0.6
Frailty, *n* (%)	221 (45.9)	151 (47.5)	11 (12.9)	59 (74.7)	<0.01
EuroSCORE II, %; mean (SD)	9.3 (9.7)	9.7 (11.0)	5.7 (4.0)	11.4 (7.3)	<0.01
STS score, %; mean (SD)	5.9 (2.0)	6.0 (2.1)	3.6 (1.7)	7.1 (2.6)	<0.01

Abbreviations. TAVR—transcatheter aortic valve replacement; SAVR—surgical aortic valve replacement; OMT—optimal medical therapy; BMI—body mass index, NYHA—New York Heart Association; CAD—coronary artery disease; TIA—transient ischemic attack, MI—myocardial infarction; PCI—percutaneous coronary intervention; CABG—coronary artery bypass grafting; VS—valvular surgery; MR—mitral regurgitation; TR—tricuspid regurgitation; PAD—peripheral artery disease, CKD—chronic kidney disease; COPD—chronic obstructive pulmonary disease; PH—pulmonary hypertension; EuroSCORE II—European System for Cardiac Operative Risk Evaluation II; STS score—Society of Thoracic Surgeons score.

Table 2. Echocardiographic parameters before and after Heart Team (HT) decisions implantation.

	Baseline					At Discharge				
Echocardiographic Parameter	**Overall (483)**	**TAVR (318)**	**SAVR (85)**	**OMT**	**p Value**	**Overall (377)**	**TAVR (298)**	**SAVR (79)**	**OMT (79)**	**p Value**
LVEF, %; mean (SD)	52.5 (13.4)	54.2 (12.5)	56.5 (12.1)	41.6 (12.5)	<0.01	55.9 (10.6)	55.4 (10.9)	57.3 (9.9)	-	0.2
LVEDD, cm; mean (SD)	5.3 (0.78)	5.2 (0.76)	5.3 (0.82)	5.4 (0.79)	0.16	5.2 (0.80)	5.2 (0.78)	5.0 (0.85)	-	0.03
LVESD, cm; mean (SD)	3.2 (0.79)	3.2 (0.77)	3.2 (0.81)	3.3 (0.82)	0.63	3.2 (0.76)	3.2 (0.76)	3.2 (0.78)	-	0.76
IVSD, cm; mean (SD)	1.36 (0.18)	1.35 (0.18)	1.39 (0.16)	1.33 (0.19)	0.11	1.33 (0.17)	1.33 (0.18)	1.34 (0.16)	-	0.76
AVA, cm^2; mean (SD)	0.78 (0.15)	0.79 (0.16)	0.76 (0.14)	0.77 (0.13)	0.25	1.78 (0.40)	1.77 (0.41)	1.82 (0.37)	-	0.44
AVA I, cm^2/m^2; mean (SD)	0.47 (0.18)	0.45 (0.16)	0.49 (0.18)	0.53 (0.20)	<0.01	0.97 (0.24)	0.96 (0.25)	0.99 (0.18)	-	0.51
PAV, m/s; mean (SD)	4.38 (0.94)	4.34 (0.94)	4.59 (0.97)	4.32 (0.91)	0.07	2.23 (0.79)	2.27 (0.74)	2.16 (0.89)	-	0.19
DVI; mean (SD)	0.20 (0.05)	0.20 (0.05)	0.21 (0.04)	0.20 (0.06)	0.39	0.41 (0.09)	0.40 (0.09)	0.45 (0.08)	-	<0.01
Peak AVG, mmHg; mean (SD)	68.6 (24.5)	69.2 (26.4)	70.3 (20.7)	64.2 (19.6)	0.21	20.3 (7.6)	21.2 (7.4)	17.3 (7.5)	-	<0.01
Mean AVG, mmHg; mean (SD)	42.6 (16.3)	42.3 (16.4)	45.4 (12.6)	41.0 (19.2)	0.18	12.4 (6.0)	12.7 (6.0)	11.3 (5.7)	-	0.07
Bicuspid valve, n (%)	40 (8.3)	20 (6.3)	13 (15.3)	7 (8.9)	0.03	-	-	-	-	-
≥Moderate PVAR, n/all (%)	-	-	-	-	-	5 (1.3)	5 (1.7)	0 (0.0)	-	0.25
≥Moderate total AR, n/all (%)	-	-	-	-	-	9 (2.4)	8 (2.7)	1 (1.3)	-	0.46

Abbreviations. TAVR—transcatheter aortic valve replacement; SAVR—surgical aortic valve replacement; OMT—optimal medical therapy; LVEF—left ventricular ejection fraction; LVEDD—left ventricular end-diastolic diameter; LVESD—left ventricular end-systolic diameter; IVSD—intraventricular septum diameter; AVA—aortic valve area; AVA I—indexed aortic valve area; PAV—peak aortic velocity; DVI—doppler velocity index; AVG—aortic valve gradient; PVAR—paravalvular aortic regurgitation; AR—aortic regurgitation.

3.4. Quality of Life

Quality of life and general health status assessed before implementing HT decisions—PCS, MCS and total—did not statistically differ between treatment strategies ($p > 0.01$ for all). At the EOF the results of PCS, MCS and total for all alive participants were significantly the lowest for SAVR, then for TAVR and the highest for OMT-group ($p < 0.05$)—detailed in Table 4. Additionally, the subanalysis of patients with active or previous cancer demonstrated that for this subgroup patients qualified for OMT had noninferior initial, but significantly worse final (EOF) quality of life (total and components) as compared with interventional strategies ($p < 0.01$). No significant differences in quality of life before and after HT evaluation were observed between TAVR and SAVR. According to the Polish version of the questionnaire, with a maximum of 103 points for PCS and 68 points for MCS (171 points—total), the highest point value means the lowest quality of life assessment, while the lowest point value indicates the highest level of quality of life.

Table 3. Primary and secondary endpoints.

Endpoints	TAVR (318)	SAVR (85)	OMT (79)	*p* Value Overall	TAVR vs. SAVR HR [95% CI]; *p*	SAVR vs. OMT HR [95% CI]; *p*	TAVR vs. OMT HR [95% CI]; *p*
Primary Endpoint, *n* (%)	110 (34.6)	28 (32.9)	75 (94.9)	<0.01	1.05 [0.73–1.51]; 0.78	0.35 [0.22–0.55]; < 0.01	0.36 [0.25–0.53]; <0.01
Secondary Endpoints, *n* (%)							
All-cause mortality	50 (15.7)	14 (16.5)	29 (36.7)	<0.01	0.95 [0.55–1.65]; 0.88	0.45 [0.22–0.90]; <0.01	0.43 [0.24–0.75]; <0.01
Non-fatal strokes	18 (5.7)	7 (8.2)	11 (13.9)	0.04	0.69 [0.29–1.65]; 0.38	0.59 [0.19–1.81]; 0.25	0.41 [0.17–1.00]; 0.01
Non-fatal disabling strokes	9 (2.8)	4 (4.7)	8 (10.1)	0.02	0.60 [0.19–1.89]; 0.39	0.46 [0.11–2.02]; 0.19	0.28 [0.09–0.91]; <0.01
CV death	36 (11.3)	9 (10.6)	19 (24.1)	<0.01	1.07 [0.55–2.06]; 0.85	0.44 [0.19–1.02]; 0.02	0.47 [0.24–0.93]; <0.01
Non-fatal MI	9 (2.8)	3 (3.5)	8 (10.1)	0.01	0.80 [0.25–2.60]; 0.74	0.35 [0.08–1.57]; 0.09	0.28 [0.08–0.94]; <0.01
AKI (30 days)	9 (2.8)	12 (14.1)	-	-	0.20 [0.07–0.57]; <0.01	-	-
New onset AF (30 days)	24 (7.5)	13 (15.3)	2 (2.5)	<0.01	0.49 [0.21–1.14]; 0.03	6.04 [2.06–17.73]; <0.01	2.98 [1.25–7.09]; 0.11
New onset AF (EOF)	38 (11.9)	19 (22.4)	10 (12.7)	0.05	0.53 [0.28–1.02]; 0.01	1.77 [0.78–4.02]; 0.11	0.94 [0.49–1.83]; 0.86
Major bleeding (30 days)	19 (6.0)	11 (12.9)	-	-	0.46 [0.19–1.11]; 0.02	-	-
Major bleeding (EOF)	36 (11.3)	17 (20.0)	1 (1.3)	<0.01	0.57 [0.28–1.16]; 0.04	15.80 [6.33–39.45]; <0.01	8.94 [4.28–18.67]; <0.01
Major vascular complications (30 days)	32 (10.06)	2 (2.35)	-	-	4.28 [2.21–8.29]; 0.02	-	-
Infective valve endocarditis (30 days)	5 (1.6)	1 (1.2)	-	-	1.33 [0.19–9.50]; 0.79	-	-
Infective valve endocarditis (EOF)	8 (2.5)	3 (3.5)	3 (3.8)	0.78	0.71 [0.18–2.90]; 0.61	0.93 [0.15–5.61]; 0.93	0.66 [0.16–2.81]; 0.54
Permanent pacemaker implantation (30 days)	53 (16.7)	6 (7.1)	-	-	2.36 [1.26–4.41]; 0.03	-	-
Permanent pacemaker implantation (EOF)	72 (22.6)	9 (10.6)	6 (7.6)	0.01	2.14 [1.22–3.76]; 0.01	1.39 [0.68–2.87]; 0.51	2.98 [1.67–5.32]; <0.01
Aortic valve re-interventions (EOF)	6 (1.9)	2 (2.4)	-	-	0.80 [0.15–4.38]; 0.78	-	-
Non-fatal rehospitalizations for AS (EOF)	51 (16.0)	10 (11.8)	38 (48.1)	<0.01	1.36 [0.80–2.31]; 0.33	0.24 [0.12–0.48]; <0.01	0.33 [0.19–0.57]; <0.01
In-hospital mortality	20 (6.3)	6 (7.1)	-	-	0.89 [0.35–2.29]; 0.8	-	-
ICU stay, days (SD)	1.8 (3.8)	4.2 (3.7)	-	-	<0.01	-	-

Abbreviations. AS—aortic stenosis; TAVR—transcatheter aortic valve replacement; SAVR—surgical aortic valve replacement; OMT—optimal medical therapy; CV—cardiovascular; MI—myocardial infarction; AKI—acute kidney injury; AF—atrial fibrillation; ICU—intensive care unit; EOF—end of follow-up.

Table 4. The quality of life before and after Heart Team (HT) decisions implementation.

	TAVR (318/268)	SAVR (85/71)	OMT (79/50)	*p*-Value
Physical Component Summary (PCS)				
Before SAVR, TAVR, HT disscusion; mean (SD)	81.5 (14.4)	79.2 (16.5)	83.1 (13.0)	0.22
After SAVR, TAVR, HT disscusion—at the end of follow up; mean (SD)	69.5 (13.9)	65.7 (16.1)	84.1 (12.5)	<0.01
Mental Component Summary (MCS)				
Before SAVR, TAVR, HT disscusion; mean (SD)	52.9 (8.6)	52.1 (9.8)	53.8 (7.8)	0.46
After SAVR, TAVR, HT disscusion—at the end of follow up; mean (SD)	41.4 (8.3)	39.1 (9.2)	56.5 (8.0)	<0.01
Total				
Before SAVR, TAVR, HT disscusion; mean (SD)	134.5 (17.5)	131.3 (20.2)	136.9 (13.8)	0.12
After SAVR, TAVR, HT disscusion—at the end of follow up; mean (SD)	111.0 (16.9)	104.8 (21.0)	140.6 (13.5)	<0.01

Abbreviations. TAVR—transcatheter aortic valve replacement; SAVR—surgical aortic valve replacement; OMT—optimal medical therapy; HT—Heart Team.

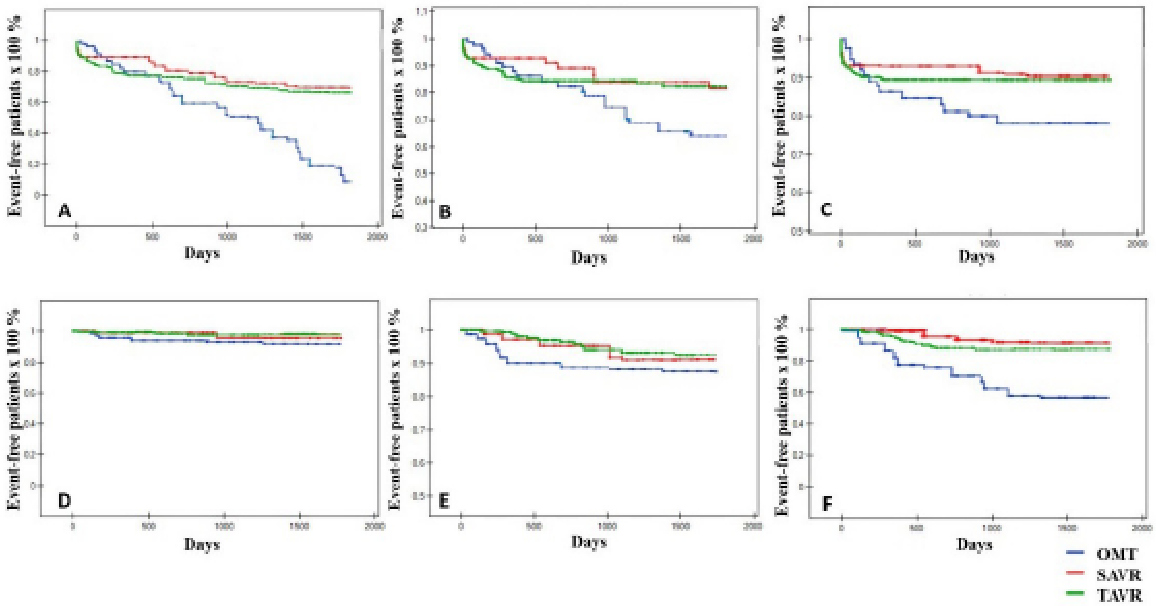

Figure 2. The Kaplan–Meier curves for endpoints. AS—aortic stenosis; TAVR—transcatheter aortic valve replacement; SAVR—surgical aortic valve replacement; OMT—optimal medical therapy; (**A**)—primary endpoint; (**B**)—all-cause mortality; (**C**)—CV (cardiovascular) death; (**D**)—non-fatal MI (myocardial infarction); (**E**)—non-fatal strokes; (**F**)—non-fatal rehospitalizations due to AS.

4. Discussion

Although risk assessment appears to be a crucial element in the appropriate preprocedural selection of the optimal management strategy for patients with AS, there are limitations to the scoring system used to estimate the risk of adverse outcomes and numerical other conditions should be evaluated to properly choose the best treatment option. Some studies suggest that the Heart Team approach may positively impact adherence to guideline-directed therapy, encourage the incorporation of patient preferences through the use of shared decision making, and improve overall outcomes [17,18]. There is recognition; however, for AS-patients, there are no randomized trials to support this approach; [19] rather, a single study describe outcomes of a multidisciplinary approach without a comparator [20].

In our opinion, only the cooperation of HT (where the risk assessment is only a component) provides a complex decision-making with appraisal of factors not routinely included in risk algorithms, which is the best to reflect the circumstances of real-world clinical practice. Although TAVR is an alternative to surgery in patients with severe symptomatic AS, there are still limited data on long-term clinical outcomes and bioprosthetic-valve function after TAVR as compared with SAVR [21–23]. Even more importantly, more clinical trials comparing treatment options for AS-patients mainly focus on interventional strategy and neglect the long-term outcomes and quality of life of patients enrolled to conservative management after HT evaluation. Only in few reports some data concerning this issue are available [8,9,14–16]. In our experience, such a cohort of patients consulting due to AS is quite large and the problem of their future care remains pressing. Hence, in our real-world clinical study, we decide to take into account all above lack in evidence regarding the importance of HT for AS-patients management.

Through our study, we would like to highlight the need for research to recognize the HT definition and range of functioning by which it can be assessed in order to advance our comprehension of the optimal care model for AS-patients. We emphasize that only HT with combination of many years' clinical practice can lead to the long-term outcomes widely assigned to result from a HT approach. For now, the HT in the present sense is often cited as derived from two randomized trials comparing PCI and CABG in CAD—SYNTAX [24] and AS—PARTNER [25,26]. In these trials, a HT was used for selection of appropriate patients during eligibility screening. In the study of Leon MB et al. [25] for 358 patients with severe AS, who were no suitable candidates for surgery, TAVR was compared with standard medical therapy (including balloon aortic valvuloplasty) and at 1 year was demonstrated to significantly reduced the rates of overall mortality (30.7% vs. 50.7% with standard therapy; HR = 0.55, 95% CI 0.40–0.74, $p < 0.001$), the composite endpoint of overall mortality or rehospitalization (42.5% vs. 71.6% with standard therapy; HR = 0.46, 95% CI 0.35–0.59, $p < 0.001$), and HF symptoms—NYHA III or IV (25.2% vs. 58.0% with standard therapy, $p < 0.001$), despite the higher incidence of major strokes and major vascular events. Further [26], for high-risk patients at 1 year, TAVR was associated with similar rates of death from any cause (24.2% vs. 26.8%, $p = 0.44$), cardiac death (14.3% vs. 13.0%; $p = 0.63$), repeat hospitalization (18.2% vs. 15.5%, $p = 0.38$), major stroke (5.1% vs. 2.4%, $p = 0.07$) and MI (0.4% vs. 0.6%, $p = 0.69$) as compared to SAVR, while vascular complications were significantly higher in TAVI-group (18.0% vs. 4.8%, $p < 0.001$) and major bleeding in SAVR-group (25.7% vs. 14.7%, $p < 0.001$). At 1 year, no statistically significant differences in reducing of HF symptoms were observed between compared groups. However, the effectiveness of HT approach on clinical outcomes or life quality was not tested in these [25,26] trials. There are several methodological strengths in this study that reinforce the validity of the obtained results: all-comer nature, retrospective enrolment, systematic and meticulous patient assessment, complete median 2.5-years clinical follow-up, assessment of quality of life and the use of standardized definitions and endpoints for clinical outcomes. To highlighted benefits of our study: we assessed all treatment options for AS-management: TAVR, SAVR and OMT with the worst long-term outcomes in primary and secondary end-points for patients qualified for non-interventional treatment (OMT). Additionally, general health status, PCS and MCS were also the poorest for OMT-patients. These results emphasized the first and foremost implications of our study: for AS-patients the intervention (SAVR or TAVR) is without doubt worth considering and despite peri- and after-procedural complications could lengthen survival and improve quality of life. Moreover, quite a large group of patients (as regards the conditions of single-center study) and the median 2.5-years of follow up is sufficient to determine with high probability that decisions of our HT are adequate and consistent with clinical practice. Furthermore, properly selected endpoints, clearly reflecting the most common and serious complications of VHD-interventional treatment, prove the translatability of the obtained results on proper functioning of HT.

5. Conclusions

In this study, we raised the role of HT in decision-making process for patients with AS demonstrating that those qualified by our internal HT for interventional strategy achieved greater benefits in both endpoints and long-term quality of life as compared to pharmacological treatment only arm. These results require further confirmation in longer follow-up or multicenter studies and registers, but surely provide establishment of HT role both in clinical practice and guidelines for AS management.

6. Limitations

The main limitations of this study is its retrospective, non-randomized character and single-center design. Above that, the decision-making process must be assigned to our individual HT cooperation and cannot be considered as a general one. Additionally, proper and regular use of drugs by patients often remains a matter of trust, hence it is difficult to determine the credibility of the endpoints in the OMT-group. Moreover, patients with non-implemented decisions were not included into final analysis, so we do not have data of their follow-up.

Author Contributions: S.J. conceived the concept of the study. S.J., M.M., E.P.-P., Ž.H., J.K., P.S., P.C., R.W., P.H., G.O., M.G. and T.M. contributed to the design of the research and data collection. S.J. analyzed the data. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to any accessible repository.

Conflicts of Interest: The authors declare no conflict of interest.

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8.2. Long-term outcomes and quality of life following implementation of dedicated mitral valve Heart Team decisions for patients with severe mitral valve regurgitation in tertiary cardiovascular care center.

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Authors: Szymon Jonik, Michał Marchel, Ewa Pędzich-Placha, Arkadiusz Pietrasik, Adam Rdzanek, Zenon Huczek, Janusz Kochman, Monika Budnik, Radosław Piątkowski, Piotr Ścisło, Janusz Kochanowski, Paweł Czub, Radosław Wilimski, Piotr Hendzel, Marcin Grabowski, Krzysztof J. Filipiak, Grzegorz Opolski, Tomasz Mazurek

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Long-term outcomes and quality of life following implementation of dedicated mitral valve Heart Team decisions for patients with severe mitral valve regurgitation in tertiary cardiovascular care center

Szymon Jonik et al., Heart Team decisions for mitral regurgitation

Szymon Jonik[1]*, Michał Marchel[1]**, Ewa Pędzich-Placha[1], Arkadiusz Pietrasik[1], Adam Rdzanek[1], Zenon Huczek[1], Janusz Kochman[1], Monika Budnik[1], Radosław Piątkowski[1], Piotr Ścisło[1], Janusz Kochanowski[1], Paweł Czub[2], Radosław Wilimski[2], Piotr Hendzel[2], Marcin Grabowski[1], Krzysztof J. Filipiak[1], Grzegorz Opolski[1], Tomasz Mazurek[1]**

[1]1st Department of Cardiology, Medical University of Warsaw, Poland

[2]Department of Cardiac Surgery, Medical University of Warsaw, Poland

Address for correspondence: Tomasz Mazurek, MD, PhD, 1st Department of Cardiology, Medical University of Warsaw, ul. Banacha 1a, 01–267 Warszawa, Poland, tel: +48 22 599 19 58, fax: +48 22 599 19 57, e-mail: tomaszmazurek.wum@gmail.com

**First author: Szymon Jonik, MD, **These senior authors contributed equally to this manuscript.*

ABSTRACT

Background: This study was purposed to investigate which treatment strategy was associated with the most favourable prognosis for patients with severe mitral regurgitation (MR) following Heart Team (HT)-decisions implementation.

Methods: In this retrospective study, long-term outcomes of patients with severe MR qualified after HT discussion to: optimal medical treatment (OMT) alone, OMT and MitraClip (MC) procedure or OMT and mitral valve replacement (MVR) were evaluated. The primary endpoint was defined as cardiovascular (CV) death and the secondary endpoints included all-cause mortality, myocardial infarctions (MI), strokes, hospitalizations for heart failure exacerbation and CV events during a mean (standard deviation [SD]) follow-up of 29 (15) months.

Results: From 2016 to 2019, 176 HT meetings were held and a total of 157 participants (mean age [SD] = 71.0 [9.2], 63.7% male) with severe MR and completely implemented HT decisions (OMT, MC or MVR for 53, 58 and 46 patients, respectively) were included into final analysis. Comparing OMT, MC and MVR groups statistically significant differences between the implemented procedures and occurrence of primary and secondary endpoints with the most frequent in OMT-group were observed ($p < 0.05$). However, for interventional strategy MC was non-inferior to MVR for all endpoints ($p > 0.05$). General health status assessed at the end of follow-up were significantly the lowest for MVR, then for MC and the highest for OMT-group ($p < 0.01$).

Conclusions: In the present study it was demonstrated that after careful HT evaluation of patients with severe MR at high risk of surgery, percutaneous strategy (MC) can be considered as equivalent to surgical treatment (MVR) with non-inferior outcomes.

Key words: Heart Team, mitral regurgitation, heart failure, mitral valve replacement, MitraClip

INTRODUCTION

Mitral regurgitation (MR) — the most common valvular heart disease (VHD) in adults and the second most frequent indication for valve surgery in Europe — despite enormous development of medicine and pharmacotherapy, still remains a pressing problem of today's cardiology, associated with the development of heart failure (HF), poor prognosis and increased mortality [1–3]. Hence the concept of multi-specialist group — the Heart Team (HT) — responsible for management of patients who are at high surgical risk or qualified only for medical therapy is still evolving. With the development of new technologies and novel approaches many patients can be successfully treated , but advanced age and/or multiple co-morbidities often make it difficult or even impossible to obtain treatment goals of care in real clinical practice. Therefore, the necessity of HT creation was recognized and the role of HT in decisions-making for patients with VHD, including MR was emphasized both in the European and American guidelines [2, 3]. An approach of a multidisciplinary experienced team, taking into account clinical, angiographic and echocardiographic data, risk stratification, long-term prognosis and patients preferences seems to be a rational tool when deciding on the best treatment method for each patient, burdened with many co-morbidities. However, the idea of HT is generally considered in the medical society as an optimal therapeutic option for "difficult" patients, its concept is still not yet widely adopted and the supportive data in the literature is insufficient and poorly proved. According to available literature, only two research papers regarding the influence of HT decisions on prognosis of MR-patients were revealed.[4, 5]. Notwithstanding, the results of these two are ambiguous and require further confirmation. More evidence investigating HT consistency and significance of decisions making and performance on hard clinical endpoints are required. We believe that the obtained results and conclusions formulated will be supportive for emphasizing the evidence-based role of HT in real-life clinical practice and its further development in the field of cardiovascular medicine.

METHODS

This single-center cohort study was conducted in the 1st Department of Cardiology, Medical University of Warsaw, a large third-degree academic centre. A total number of 254 patients consulted for symptomatic, both primary (PMR) and secondary (SMR) MR during 176 HT meetings in 2016–2019 were enrolled in this retrospective study. The inclusion criteria were: aged ≥ 18 years and complete clinical, echocardiographic and angiographic characteristics. The exclusion criteria included the following: pregnancy/lactation, disseminated neoplastic process, life expectancy < 1 year, lack of informed, written consent. All of patients were presented to an experienced HT–council consisting of at least four specialists: general (conservative) cardiologist, echocardiographer, interventional cardiologist and cardiac surgeon. Patients were qualified after HT discussion to one of three main strategies: optimal medical treatment (OMT) alone, OMT and MitraClip (MC) procedure or OMT and mitral valve replacement (MVR). OMT was defined as use of drugs in a manner that provides an optimal reduction of signs and symptoms associated with mitral valve (MV) defect or secondary to subsequent HF. The degree of MR was assessed using ventriculographic criteria on a scale from 1 to 4, where 1+ was determined as faint opacification of the left atrium (LA) with clearing of contrast during each beat, while 4+ meant immediate, dense opacification of the LA with filling of the pulmonary veins. The severe MR in the present study was defined as grade 3+ or 4+ and effective regurgitant orifice (ERO) ≥ 0.40 cm^2 for severe PMR and ERO ≥ 0.20 cm^2 for severe SMR assessed by echocardiography (in accordance to European guidelines) [2]. The severity of HF symptoms was assessed using New York Heart Association (NYHA) classification, chronic kidney disease (CKD) defined as glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2, anemia as hemoglobin level < 12 g/dL for women and < 14 g/dL for men, cancer — as active or up to 5 years prior and smoking — as active or in the past. Ultimately, after excluding non-eligible patients, the patients who died before decision implementation, did not consent with HT decision or loss of follow-up, 157 (61.8%) individuals with completely implemented HT decisions (OMT, MC, MVR — 53, 58, 46 patients, respectively) were included into the final analysis. As the primary endpoint of cardiovascular (CV) death was considered, while overall mortality, non-fatal myocardial infarctions (MI), non-fatal strokes, non-fatal hospitalizations for HF exacerbation and any CV events (including CV death, non-fatal MI, non-fatal stroke and non-fatal hospitalizations for HF exacerbation) per single patient were assessed as secondary endpoints. All participants were observed for occurrence of endpoints with mean ± standard deviation (SD) follow-up of 29 ± 15 months. The main outline of the study was presented in Figure 1. Additionally, general health status, using the short-form (SF)-36 questionnaire (totally and separately for physical component summary [PCS] and mental component summary [MCS]) before MVR, MC and HT discussion (for patients qualified for OMT) and at the end of follow-up for all living participants (31 December 2020) was assessed. Due to the observational nature of the study, an application to the ethical/institutional review board (IRB) for approval of the present study was unnecessary. All participants gave written informed consent for publication of study results.

Statistical analysis

The PQStat software (version 1.6.6, PQStat, Poznan, Poland) was used for statistical analysis. The normality of distribution for continuous variables was confirmed with the Shapiro–Wilk test. Categorical data were expressed as counts and percentages, while continuous data were presented as mean ± SD. The comparison between groups of patients qualified for individual treatment strategies was performed using chi-square test and the statistical analysis was executed using one-way analysis of variance (ANOVA). To compare the outcomes for all strategies with each other, the hazard ratios (HRs) with 95% confidence intervals (95% CI) were calculated. Time to event analysis was performed using Kaplan–Meier curves. All p values (p) were given to at least two-sided and p value lower than 0.05 were considered statistically significant.

RESULTS

Study population

From January 2016 to December 2019, 176 HT meetings were held and total of 157 patients with severe MR met inclusion and exclusion criteria with completely implemented HT decisions (100; 63.7%) male, age (years, mean ± SD) = 71.0 ± 9.2, body mass index (kg/m^2, mean ± SD) = 26.2 ± 4.8, 43 (27.4%) with primary MR, 154 (98.1%) with HF, NYHA (class, mean ± SD) = 3.50 ± 0.50, European System for Cardiac Operative Risk Evaluation II (EuroSCORE II, %, mean ± SD) = 7.71 ± 2.55 and given co-morbidities were followed up. The mean delay time from HT decision to implementation was: 59 ± 9 and 31 ± 6 days for MC and MVR, respectively ($p = 0.001$). As regards statistically significant differences between MVR, MC and OMT groups, patients who qualified for OMT were older than those with implemented MVR or MC, primary MR was the most common in MVR-group, while participants with MC had the most severe symptoms (assessed by NYHA class). Diabetes, atrial fibrillation (AF) and chronic obstructive pulmonary disease (COPD) were the most common in OMT-group, while CKD and history of previous coronary artery bypass grafting were most often found in MC-group ($p < 0.05$ for all). Participants qualified for MVR had the lowest perioperative risk of death as assessed using the EuroSCORE II scale ($p < 0.05$) — detailed in Table 1.

Echocardiographic parameters

All patients were assessed by echocardiography — from OMT-group at the time of HT discussion and from MVR- and MC-groups before and after intervention (at the time of discharge from the hospital). Statistically significant differences in echocardiographic parameters before HT decision implementation were observed in the following: ejection fraction of left ventricle (LVEF) with the highest in MVR-group, the diameter of LV (assessed by left ventricular end-diastolic dimension [LVEDD]) and ERO with the lowest in MVR-group and mean mitral valve gradient (MVG) — the lowest in MC-group ($p < 0.05$ for all). The results of echocardiographic parameters assessed after MVR or MC implementation differ between these two groups for residual central MR degree ≥ 2 and paravalvular leak (PVL), ERO, MR volume, maximum and mean MVG and were significantly better in MVR-group ($p < 0.05$ for all) — as detailed in Table 2.

Endpoints

In-hospital mortality did not significantly differ between MVR and MC strategy (4 [8.7%] vs. 1 [1.7%]; $p = 0.10$). The occurrence of primary endpoint was statistically the most frequent in OMT-group (20 patients, 37.7%), while in MVR and MC groups — 7 (15.2%) and 10 (17.2%) patients, respectively ($p = 0.01$). Additionally, MVR and MC were found to be significantly superior to OMT for all secondary endpoints ($p < 0.05$ for all endpoints) — detailed in Table 3. However, for interventional strategy — no statistically significant differences between MVR and MC outcomes were observed ($p > 0.05$ for all endpoints). The Kaplan-Meier curves for primary and secondary endpoints were presented in Figure 2.

Quality of life

General health status before implementing HT decisions — PCS, MCS and total — did not statistically differ between treatment groups ($p > 0.05$ for all). At the end of follow-up the results of PCS, MCS and total for all living participants were significantly the lowest for MVR, then for MC and were the highest for OMT-group ($p < 0.01$) — detailed in Table 4. According to the Polish version of the questionnaire, with a maximum of 103 points for PCS and 68 points for MCS (171 points — total), the highest point value means the lowest quality of life assessment, while the lowest point value indicates the highest level of quality of life [6, 7].

DISCUSSION

Mitral regurgitation caused by any structural or functional dysfunction of MV leaflets, MV apparatus or LV remodeling is a common problem of patients admitted to cardiology divisions all over the world [1–3, 8]. Regardless of the mechanism of this defect, MR results in the progression of HF symptoms, deterioration of the quality of life and increased mortality, even despite the surgical and pharmacological treatment applied [1–3]. With an aging population, living with more chronic medical conditions, the frequency of this disease will continue to grow, as will be questions about new treatment options. Current evidence concerning survival outcomes of MR-patients qualified for different treatment modalities remains scarce, and although multiple reports have published survival data, only a few have compared outcomes post MC to surgical treatment. So far, only one randomized controlled trial (RCT), the Endovascular Edge-to-Edge Repair Study (EVEREST) II and some observational studies evaluating prognosis after conventional surgery versus MC were reported. In the EVEREST II trial [9] patients with grade 3/4+ MR were randomly assigned to MC or conventional MV surgery in a 2:1 ratio (178:80). At 5 years the rate of the composite endpoint of freedom from death, surgery for residual MR, or 3/4+ MR in the intention-to-treat population was 44.2% vs. 64.3% in the MC and surgical groups, respectively ($p = 0.01$). Five-year mortality rates were 20.8% and 26.8% ($p = 0.4$) for percutaneous repair and surgery, respectively, whereas in multivariable analysis, treatment strategy was not associated with survival.

In the recently updated meta-analysis of Oh et al. [10] (9 studies including the EVEREST II trial) demonstrating outcomes after MR-treatment, MC-patients (n = 533) as compared to surgical group — MVR (n = 644) had at baseline more comorbidities, further — residual moderate-to-severe MR was more frequent in MC-cohort both at discharge (OR = 2.81; $p < 0.01$) and at 5 years (OR = 2.46; $p < 0.01$) and the higher need for reoperation in MC-group at latest follow-up (OR = 5.28; $p < 0.01$) was observed. However, overall mortality was comparable between these two groups ($p = 0.06$) for a mean follow-up of 4.8 years.

Based on current European recommendations for MR-treatment the role of HT is poorly underlined with class IIb and level C, while in American guidelines with class IIa/b from nonrandomized trials [2, 3]. There is growing evidence confirming the multidisciplinary approach of HT for management of many CV diseases — coronary artery disease [11–15], aortic stenosis [16–20] and AF [21] which has demonstrated great merit. Only for the safety and efficacy of the HT concept in MR filling the gaps with evidence is still urgent, whereas only two papers on this issue are currently available in the literature [4, 5]. In the study of Heuts et al. [4] 158 patients with MR qualified by HT to different treatment strategies 30-day mortality for surgery (isolated MVR and concomitant surgery — 67 patients), transcatheter intervention (MC or MVP — 20 patients) and conservative groups (71 patients) were 3 (4.4%), 0 (0.0%) and 3 (4.2%), respectively. Using the Kaplan-Meier curves at a median follow-up of 450 days for the various groups, a beneficial long-term survival for surgically treated patients was demonstrated [4]. In other research, Külling et al. [5] reported retrospective single-center cohort study of 400 patients treated for MR. As followed by HT decisions, 179 (44.8%) patients were treated using MC, 185 (46.2%) by MVP and 36 (9.0%) by MVR. Outcomes with a mean follow-up time of 32.2 ± 17.6 months revealed that patients treated with MVP had higher 4-year survival (HR 0.40; 95% CI 0.26–0.63; $p < 0.001$) and fewer combined endpoints [5]. The present research is one of the few studies involving the concept of HT for MR-patients and according to available literature, the first study in which the MR-patients quality of life following HT decisions and implementation was also assessed. Contrary to expectations created by guidelines for VHD [2, 3], where the surgical approach (MV-repair whenever possible) is a gold standard of treatment for MR-patients, in the current study the percentage of patients for whom surgical therapy following HT discussion was chosen and implemented was only 29.3%, while 36.9% received percutaneous therapy (MC) and 33.8% were disqualified from interventional strategy (OMT). What seems to be even more important, participants treated with MC compared with MVR-group were not statistically significant, but had lower in-hospital mortality, while MC strategy was non-inferior to MVR for primary and secondary endpoints. As expected, mainly participants with primary MR, acceptable valve anatomy and lower surgical risk were qualified for surgical treatment (MVR), while those with secondary MR and increased risk were treated with MC. Regardless the results obtained herein, and although all of treatment strategies were proven to be effective in reducing MR, it should be clearly emphasized that the efficacy of MVR, MC and OMT is highly dependent on patient selection. For individuals with primary MR (basically dysfunction of MV, commissural disease, perforations, clefts), mitral valve area < 3.0 cm^2, high mean MVG (> 5 mmHg), at early stage of LV remodeling, not at critically-high risk of cardiac surgery (i.e. LVEF > 30%, LVEDD < 7.0 cm, without severe PH, end-stage renal disease or on dialysis), without bleeding/coagulation disorders (need for anticoagulation after MVR) and indications for concomitant surgery of other valve or coronary artery bypass grafting, the MVR is the preferred method of treatment. On the other side, there are severely burdened patients with a high risk of death associated with classical MVR. These of them with "disproportionate" MR (regurgitant volumes disproportionately higher than the degree of LV dilatation), with no calcification of MV, optimally mitral valve area > 3.0 cm^2 and mean MVG < 4 mmHg are likely to mainly benefit from a therapy targeted to MC. At this point, the incidence of iatrogenic atrial septal defect after MC procedure should be also stressed out. This kind of MC consequence, if persistent can lead to stroke, right-sided heart enlargement, worse tricuspid regurgitation, and a higher re-hospitalization rate for HF [22]. Finally, the present study had older patients with more advanced HF, NYHA class IV and severe tricuspid regurgitation who had a dismal prognosis and patients with “proportionate” MR (regurgitant volume totally commensurate to LV enlargement). These subgroups would likely benefit the most from strategies aimed at reducing LV size (i.e., OMT and cardiac resynchronization therapy) alone, not directed to MV apparatus. As the problem of patients with MR treatment becomes more challenging, new therapeutic strategies, such as percutaneous MVR (TMVR) will be a step towards more sufficient and safe treatment. Preliminary studies reported that TMVR by compassionate use of TMVR prostheses as valve-in-valve and valve-in ring was associated with lower-than-expected peri-interventional mortality and satisfactory outcomes in highly selected patients [23–25]. Undoubtedly, the results of the current study should be followed by further RCTs, however, it was demonstrated that after careful HT evaluation, percutaneous strategy (MC) can be considered as a comparably effective and safe to surgical treatment (MVR) for some subsets of patients with severe MR. This may have an impact on recommendations towards MC in subsequent VHD guidelines.

Limitations of the study

The main limitations of this study are its retrospective character, a small sample size, and single-center design. Above that, the decisions-making process must be assigned to our individual HT cooperation and cannot be considered as a general one. Additionally, the treatment results for used strategies were presented together for patients with primary and secondary MR, what it does not make possible, is to clearly determine which therapeutic option is best for a given etiology. Moreover, patients with non-implemented decisions were not included into the final analysis, so data was not available on their follow-up.

Patients were not matched; hence comparison of groups should be considered with caution. Individuals qualified for interventional strategies differ significantly in some parameters, both clinical (especially the etiology of MR, diabetes, CKD and COPD) and echocardiographic (mostly LVEF and mean MVG), hence the obtained outcomes cannot be a contribution to formulating far-reaching and unquestionable conclusions.

CONCLUSIONS

The present study illustrates how the HT approach and decisions affect prognosis and the quality of life for patients with MR. It should be especially emphasized that for MR-patients choosing the best treatment method should never be individual and only HT seems to be a suitable tool to provide satisfactory outcomes and acceptable quality of life. Further research on this issue is required, but our initial results may state a cornerstone for the future.

Conflict of interest: None declared

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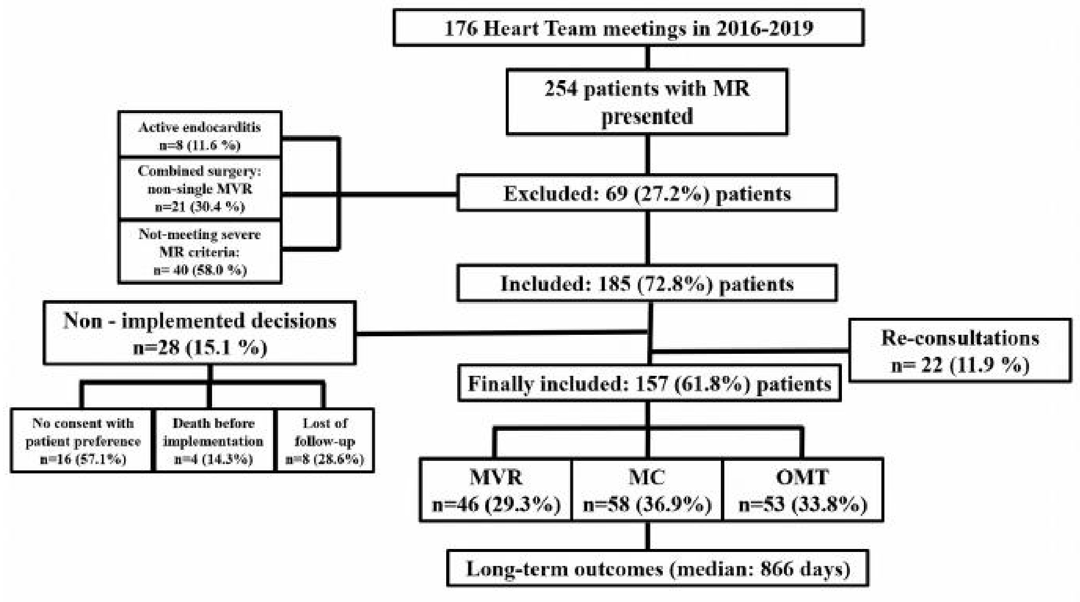

Figure 1. Study design; MR — mitral regurgitation; MVR — mitral valve replacement; MC — MitraClip; OMT — optimal medical therapy.

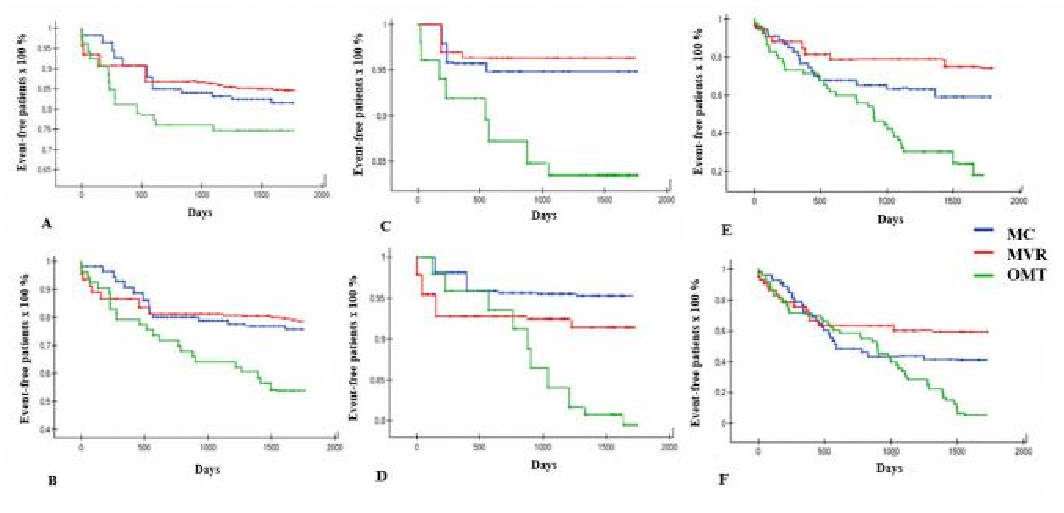

Figure 2. The Kaplan-Meier curves for endpoints; **A.** Cardiovascular deaths; **B.** Overall mortality; **C.** Non-fatal myocardial infarction; **D.** Non-fatal strokes**; E.** Non-fatal hospitalizations for heart failure exacerbation; **F.** Cardiovascular events; MC — MitraClip; MVR — mitral valve replacement; OMT — optimal medical therapy.

Table 1. Baseline clinical characteristics.

N = 157	Overall (157)	MVR (46)	MC (58)	OMT (53)	P
Age [years]	71.03 ± 9.18	67.8 ± 8.86	71.1 ± 9.72	73.7 ± 11.05	0.02
Gender — male	100 (63.7%)	31 (67.4%)	37 (63.8%)	32 (60.4%)	0.77
BMI [kg/m^2]	26.22 ± 4.76	26.76 ± 6.04	25.23 ± 13.8	26.82 ± 3.95	0.47
Etiology — primary MR	43 (27.4%)	26 (56.5%)	8 (11.9%)	9 (17.0%)	< 0.001
Heart failure	154 (98.1%)	44 (95.7%)	58 (100.0%)	52 (98.1%)	0.28
NYHA	3.50 ± 0.50	3.39 ± 0.49	3.64 ± 0.48	3.47 ± 0.50	0.03
Coronary artery disease	114 (72.6%)	29 (63.0%)	45 (77.6%)	40 (75.5%)	0.22
Diabetes	73 (46.5%)	8 (17.4%)	31 (53.4%)	34 (64.2%)	<0.001
Hypertension	148 (94.3%)	42 (91.3%)	55 (94.8%)	51 (96.2%)	0.57
Previous stroke/TIA	42 (26.8%)	14 (30.4%)	15 (25.9%)	13 (24.5%)	0.79
Atrial fibrillation	48 (30.6%)	8 (17.4%)	18 (31.0%)	22 (41.5%)	0.03
Previous MI	102 (65.0%)	24 (52.2%)	41 (70.7%)	37 (69.8%)	0.10
Previous PCI	111 (70.7%)	28 (60.9%)	43 (74.1%)	40 (75.5%)	0.22
Previous CABG	36 (22.9%)	4 (8.7%)	17 (29.3%)	15 (28.3%)	0.02
Chronic kidney failure	136 (86.6%)	33 (71.7%)	55 (94.8%)	48 (90.6%)	0.001
Anemia	122 (77.7%)	34 (73.9%)	47 (81.0%)	41 (77.4%)	0.69
Dyslipidemia	134 (85.4%)	39 (84.8%)	51 (87.9%)	44 (83.0%)	0.76
COPD	46 (29.3%)	6 (13.0%)	17 (29.3%)	23 (43.4%)	0.004
Cancer	36 (22.9%)	7 (15.2%)	13 (22.4%)	16 (30.2%)	0.21
Smoking	135 (86.0%)	40 (87.0%)	52 (89.7%)	43 (81.1%)	0.43

EuroSCORE II [%]	7.71 ± 2.55	6.65 ± 2.79	8.13 ± 2.90	8.05 ± 1.81	0.004
Medications at discharge:					
ACEI/ARB	143/152 (91.45%)	37/42 (88.10%)	51/57 (89.47%)	51/53 (96.23%)	0.16
ARNI	7/152 (4.61%)	2/42 (4.76%)	3/57 (5.26%)	2/53 (3.77%)	0.93
Beta–blockers	133/152 (87.50%)	34/42 (80.95%)	50/57 (87.72%)	49/53 (92.45%)	0.25
Loop diuretics agents	144/152 (94.74%)	38/42 (90.48%)	53/57 (92.98%)	53/53 (100.0%)	0.09
Aldosterone antagonists	75/152 (49.34%)	16/42 (38.10%)	28/57 (49.12%)	31/53 (58.49%)	0.14

MR — mitral regurgitation; MVR — mitral valve replacement; MC — MitraClip; OMT — optimal medical therapy; BMI — body mass index; NYHA — New York Heart Association; TIA — transient ischemic attack; MI — myocardial infarction; PCI — percutaneous coronary intervention; CABG — coronary artery bypass grafting; COPD — chronic obstructive pulmonary disease; EuroSCORE II — European System for Cardiac Operative Risk Evaluation II; ACEI — angiotensin-converting enzyme inhibitors; ARB — angiotensin receptor blockers; ARNI — angiotensin receptor-neprilysin inhibitors

Table 2. Echocardiographic parameters before and after Heart Team (HT) decisions implantation.

	Before Heart Team decisions implantation				
	Overall (157)	**MVR (46)**	**MC (58)**	**OMT (53)**	**P**
LVEF [%]	33.09 ± 9.54	42.43 ± 6.09	30.3 ± 11.1	30.3 ± 7.1	< 0.001
LVEDD [cm]	6.40 ± 0.66)	6.24 ± 0.65	6.36 ± 0.55	6.61 ± 0.66	0.03
MR [degree]	3.36 ± 0.48	3.35 ± 0.39	3.34 ± 0.53	3.38 ± 0.46	0.76
ERO [cm^2]	0.39 ± 0.09	0.37 ± 0.08	0.39 ± 0.11	0.42 ± 0.08	0.01
MR volume [mL/beat]	49.58 ± 12.71	48.50 ± 11.11	50.77 ± 17.33	49.46 ± 9.44	0.85

Max MVG [mmHg]	18.29 ± 8.27	17.17 ± 7.54	18.23 ± 6.24	19.24 ± 10.24	0.45
Mean MVG [mmHg]	5.80 ± 2.45	6.19 ± 2.29	4.12 ± 1.41	7.31 ± 2.36	< 0.001
	After Heart Team decisions implantation				
	MVR (42)		**MC (57)**		**P**
Central MR degree ≥ 2	0 (0.0%)		8 (14.04%)		0.01
Paravalvular leak	3 (7.1%)		14 (24.56%)		0.02
ERO [cm^2]	0.12 ± 0.01		0.20 ± 0.08		< 0.001
MR volume [mL/beat]	15.40 ± 5.28		23.23 ± 7.93		< 0.001
Max MVG [mmHg]	6.64 ± 4.14		10.28 ± 5.90		< 0.001
Mean MVG [mmHg]	2.19 ± 0.94		3.02 ± 1.34		0.01

MR — mitral regurgitation; MVR — mitral valve replacement; MC — MitraClip; OMT — optimal medical therapy; BEFORE — for MVR and MC — before procedure and for OMT — during Heart Team consultation; AFTER — after implemented procedure (MVR and MC); LVEF — left ventricular ejection fraction; LVEDD — left ventricular end-diastolic dimension; ERO — effective regurgitant orifice; MVG — mitral valve gradient

Table 3. Primary and secondary endpoints.

	MVR (46 patients)	**MC (58 patients)**	**OMT (53 patients)**	**P**
Primary endpoint				
CV death	7 (15.2%)	10 (17.2%)	20 (37.7%)	0.01
Secondary endpoints				
All-cause mortality	10 (21.7%)	14 (24.1%)	29 (54.7%)	< 0.01
Non-fatal MI	2 (4.3%)	3 (5.2%)	9 (17.0%)	0.04
Non-fatal stroke	4 (8.7%)	3 (5.2%)	11 (20.8%)	0.03

Non-fatal hospitalizations for HF	11 (23.9%)	24 (41.4%)	44 (83.0%)	< 0.01
CV events/one patient	19 (41.3%)	34 (58.6%)	51 (96.2%)	< 0.01
In-hospital mortality	4 (8.7%)	1 (1.7%)	–	0.10

MVR — mitral valve replacement; MC — MitraClip; OMT — optimal medical therapy; CV — cardiovascular; MI — myocardial infarction; HF — heart failure

Hazard ratios (HR) with 95% confidence intervals (CI) comparing all strategies with each other (HR [95% CI]; P): **In-hospital mortality:** MC vs. MVR (0.2 [0.03–1.10]; 0.10); **CV death:** MC vs. MVR (1.13 [0.44–2.56]; 0.78), OMT vs. MC (2.19 [0.69–3.07]; 0.01), OMT vs MVR (2.48 [0.69–3.53]; 0.01); **all-cause mortality:** MC vs. MVR (1.11 [0.55–2.41]; 0.78), OMT vs. MC (2.27 [0.70–2.49]; < 0.01), OMT vs. MVR (2.52 [0.77–2.99]; < 0.01); **non-fatal MI:** MC vs. MVR (1.19 [0.27–5.03]; 0.85), OMT vs. MC (3.28 [0.55–6.40]; 0.05), OMT vs. MVR (3.91 [0.58–8.31]; 0.05); **non-fatal stroke:** MC vs. MVR (0.59 [0.16–2.24]; 0.48), OMT vs. MC (4.01 [0.69–6.13]; 0.01), OMT vs. MVR (2.39 [0.38–4.02]; 0.01); **non-fatal hospitalizations for HF:** MC vs. MVR (1.73 [0.88–2.78]; 0.06), OMT vs. MC (2.0 [0.99–2.75]; < 0.01), OMT vs. MVR (3.47 [1.47–4.52]; < 0.01); **CV events/one patient:** MC vs. MVR (1.42 [0.59–1.63]; 0.08), OMT vs. MC (1.64 [1.05–2.52]; < 0.01), OMT vs. MVR (2.33 [0.95–2.67]; < 0.01)

Table 4. The quality of life before and after Heart Team (HT) decisions implementation.

	MVR (46 patients)	**MC (58 patients)**	**OMT (53 patients)**	**P value**
Physical component summary				
Before MVR, MC, HT discussion	76.15 ± 15.60%	77.84 ± 15.61	79.58 ± 11.89	0.50 (P for MVR vs. MC; MVR vs. OMT; MC vs. OMT: 0.58; 0.22; 0.51, respectively)
After MVR, MC, HT discussion — at the end of follow up	60.15 ± 14.49	68.34 ± 15.93	83.08 ± 9.44	< 0.01 (P for MVR vs. MC; MVR vs. OMT; MC vs. OMT: < 0.01 for all)
Mental component summary				
Before MVR, MC, HT discussion	51.07 ± 10.17	52.05 ± 8.43	53.81 ± 8.29	0.30 (P for MVR vs. MC; MVR vs. OMT; MC vs. OMT: 0.59; 0.14; 0.27, respectively)
After MVR, MC, HT discussion — at the end of	43.07 ± 8.79	46.55 ± 8.82	57.31 ± 6.34	< 0.01 (P for MVR vs. MC; MVR vs. OMT; MC vs. OMT: 0.06; < 0.01; <

follow up				0.01, respectively)
Total				
Before MVR, MC, HT discussion	127.22 ± 20.85	129.90 ± 19.14	133.40 ± 12.11	0.22 (P for MVR vs. MC; MVR vs. OMT; MC vs. OMT: 0.50; 0.07; 0.26, respectively)
After MVR, MC, HT discussion — at the end of follow up	103.22 ± 17.42	114.90 ± 15.99	140.40 ± 8.84	< 0.01 (P for MVR vs. MC; MVR vs. OMT; MC vs. OMT: < 0.01 for all)

MVR — mitral valve replacement; MC — MitraClip; OMT — optimal medical therapy

8.3. Optimal Management of Patients with Severe Coronary Artery Disease following Multidisciplinary Heart Team Approach—Insights from Tertiary Cardiovascular Care Center.

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Optimal Management of Patients with Severe Coronary Artery Disease following Multidisciplinary Heart Team Approach—Insights from Tertiary Cardiovascular Care Center

Szymon Jonik [1], Michał Marchel [1], Ewa Pędzich-Placha [1], Arkadiusz Pietrasik [1], Adam Rdzanek [1], Zenon Huczek [1], Janusz Kochman [1], Monika Budnik [1], Radosław Piątkowski [1], Piotr Scisło [1], Paweł Czub [2], Radosław Wilimski [2], Jakub Maksym [1], Marcin Grabowski [1], Grzegorz Opolski [1] and Tomasz Mazurek [1,*,†]

[1] 1st Department of Cardiology, Medical University of Warsaw, Banacha 1a Str., 01-267 Warsaw, Poland; szymonjonik.wum@gmail.com (S.J.); michal.marchel@wum.edu.pl (M.M.); ewa.pedzich@wp.pl (E.P.-P.); apietrasik@tlen.pl (A.P.); ardza@wp.pl (A.R.); zhuczek@wp.pl (Z.H.); jkochman@tlen.pl (J.K.); moni2911@interia.pl (M.B.); radekp1@gmail.com (R.P.); piotr.scislo@gmail.com (P.S.); jakub.maksym@gmail.com (J.M.); marcin.grabowski@wum.edu.pl (M.G.); grzegorz.opolski@wum.edu.pl (G.O.)

[2] Department of Cardiac Surgery, Medical University of Warsaw, Banacha 1a Str., 01-267 Warsaw, Poland; pczub73@gmail.com (P.C.); rwilimski@gmail.com (R.W.)

* Correspondence: tmazurek@kardia.edu.pl

† Senior author.

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Abstract: Background: The purpose of this retrospective study was to investigate outcomes of patients with severe coronary artery disease (CAD) after implementing various treatment strategies following multidisciplinary Heart Team (MHT) discussion. Methods Primary and secondary endpoints and quality of life during a mean (SD) follow-up of 37 (14) months of patients with severe CAD (three-vessel [3-VD] or/and left main [LM] disease) qualified after MHT discussion to optimal medical treatment (OMT) alone, OMT and coronary artery bypass grafting (CABG), or OMT and percutaneous coronary intervention (PCI) were evaluated. As the primary endpoint, major adverse cardiac or cerebrovascular events (MACCE) (i.e., death from any cause, stroke, myocardial infarction, or repeat/need for revascularization) were considered. Result: From 2016 to 2019, 176 MHT meetings were held, and a total of 1286 participants with severe CAD and completely implemented MHT decisions (OMT, CABG, or PCI for 251, 356, and 679 patients, respectively) were included. The occurrence of the primary endpoint was significantly increased in OMT-group (154 (61.4%) vs. CABG and PCI groups—110 (30.9%) and 302 (44.5%) patients, respectively ($p < 0.05$). For interventional strategies only—CABG was associated with reduced rates of MACCE and repeat revascularization, while the superiority of PCI for stroke and disabling stroke was observed ($p < 0.05$). The general health status assessed at the end of the follow-up was significantly better for patients who underwent CABG or PCI than in the OMT group ($p < 0.05$). Conclusions: In this real-life study, we presented a single-center experience of providing optimal medical care for patients with severe CAD following MHT discussion.

Keywords: multidisciplinary heart team; multivessel coronary artery disease; coronary artery bypass grafting; percutaneous coronary intervention; optimal medical therapy

1. Introduction

Coronary artery disease (CAD), consisting of acute coronary syndromes (ACS) and chronic coronary syndromes (CCS), is a group of clinical diagnoses related to myocardial ischemia, including the manifestation of atherosclerosis in coronary arteries, and is the most common cause of death of over 30% of people older than 35 years [1]. CAD affected 197 million people in 2019 and was generally responsible for 9.14 mil deaths [2,3].

Although age-standardized prevalence and morbidity from CAD per 100,000 persons decreased between 1980 and 2019, especially in developed countries [4,5], it remains the most serious medical problem of the modern world, significantly reducing life expectancy and quality. With a growing number of therapeutic options such as less invasive methods of cardiac surgery, the enormous development of percutaneous methods, and the availability of new drugs improving survival in CAD patients, the idea of a multidisciplinary heart team (MHT) to manage individuals with complex diseases has been implemented and still plays a central concept in the real-life care of patients with CAD (class I recommendation in European and American guidelines) [6–10]. Recently, the results of the ISCHEMIA trial demonstrated that for stable CAD patients without significant left main stenosis (LMS) and moderate to severe ischemia, initial conservative strategy (optimal medical therapy (OMT)) is non-inferior to invasive methods (coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI)) regarding the risk of ischemic cardiovascular (CV) events or death from any cause [11]. Therefore, it prompts us to seriously consider which treatment will be the most beneficial for CAD patients and whether invasive always means better, making the decision-making process difficult for individuals. However, though the idea of MHT is generally adopted in medical society, an unsatisfactory consensus on how MHT should cooperate, what desired goals are established, and most importantly, the long-term results of MHT decisions, implementation, and patients' quality of life are still poorly investigated. Some studies address the association of MHT cooperation and MVD-patients evaluation [12–21]. However, among them, there are very few randomized trials supporting this approach since studies describe outcomes of a multidisciplinary approach without a comparator. The lack of clearly expressed data calls for more evidence investigating basic MHT influence on CAD-patients management and thus CV outcomes. In this retrospective study, we try to evaluate MVD-patients management, long-term outcomes, and quality of life following implementation of MHT decisions in daily clinical practice of tertiary cardiovascular care centers. We believe that the presented results will support and emphasize the evidence-based role of MHT in the decision-making process for MVD-patients and honor the MHT concept as fundamental for linking evidence-based medicine and a multidisciplinary approach for implementing an optimal treatment among an aging and multi-burdened demographic and the rapidly evolving field of cardiovascular and pharmacological medicine.

2. Methods and Study Design

This single-center observational study was conducted in the 1st Department of Cardiology, Medical University of Warsaw, a large tertiary cardiovascular care center in Poland. A total of 1509 patients consulted for CAD during 176 MHT meetings in 2016–2019 were enrolled in this retrospective study. The inclusion criteria were: aged ≥18 years and complete clinical, echocardiographic, and angiographic characteristics. The angiographic inclusion criterium for final analysis was severe CAD, defined as three-vessel disease (3-VD) and/or left main (LM) disease. The exclusion criteria included the following: pregnancy/lactation, disseminated neoplastic process, life expectancy <1 year, lack of informed, written consent. All of the patients were evaluated in a weekly meeting by an MHT composed of at least 4 specialists: interventional cardiologist, cardiac surgeon, clinical cardiologist, and non-invasive imaging specialist (often also an anesthesiologist, intensive care specialist, radiologist, and neurologist) and qualified after MHT discussion and unanimous consent of all participating physicians to one of three main strategies: OMT alone; OMT and CABG; or OMT and PCI. To not delay the treatment for acute patients, they were discussed firstly during the meetings, and decisions were implemented immediately. Sequentially, 122 (8.1%) patients presented during MHT meetings were excluded from further analysis due to one vessel disease (1-VD) or two-vessel disease (2-VD) without LM involvement, thus not meeting angiographic criteria for severe CAD or qualification for combined surgery (CABG) and mitral and/or aortic valve surgery—85 and 37 patients, respectively. Sequentially, out of 1387 (91.9%) patients, 128 (9.2%) re-discussed cases qualified for OMT, CABG, or PCI, a total number of 101 (7.3%) participants were excluded due to no consent between MHT and patient preference, loss of follow-up, or death before implementation—58, 29, and 14 patients, respectively. Ultimately, in the final study, 1286 (85.2%) patients with completely implemented MHT decisions (OMT, CABG, PCI—251, 356, 679 patients, respectively) were included. OMT was defined as using drugs with proven impact on increased survival or providing optimal reduction of the signs and symptoms associated with CAD. The severity of CAD or Heart Failure (HF) symptoms were assessed using Canadian Cardiovascular Society (CCS) or New York Heart Association (NYHA) classifications, respectively; chronic kidney disease (CKD) defined as glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 (mL per min per 1.73 square m), severe pulmonary arterial hypertension (PAH) as pulmonary artery systolic pressure (PASP) >55 mmHg, anemia as hemoglobin level <12 g/dL for women and <14 g/dl for men (g/dL—gram/decilitre), and cancer—active or up to 5 years back. The LM disease was defined as LM stenosis >50%. As the primary endpoint, a major adverse cardiac or cerebrovascular event (MACCE) (i.e., death from any cause, stroke, myocardial infarction, or repeat/need for revascularization) at the end of follow-up (EOF) was considered, while assessed independently the components of MACCE, composite of all-cause death, MI or stroke, and cardiovascular (CV) death, disabling stroke, in-hospital mortality, and for interventional strategies—graft occlusion or stent thrombosis were determined as secondary endpoints. All participants were observed for the occurrence of endpoints with a mean follow-up (SD) of 37 (14) months. The main outline of the study is presented in Figure 1. Additionally, general health status using the short-form (SF)-36 questionnaire (totally and separately for physical component summary [PCS] and mental component summary [MCS]) before CABG, PCI, and MHT discussions (for patients qualified for OMT) and at the EOF for all living participants (31 December, 2020) was assessed. We have not yet obtained ethical/institutional review board (IRB) approval for our research. However, due to the observational nature of the study, in accordance with applicable regulation, it is not required.

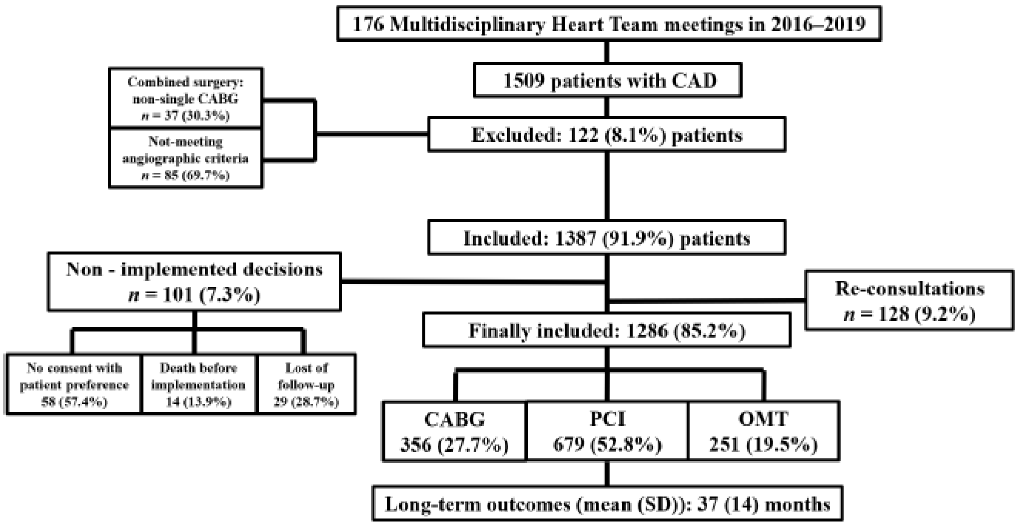

Figure 1. Study design. CAD—coronary artery disease, CABG—coronary artery bypass grafting, PCI—percutaneous coronary intervention, OMT—optimal medical therapy.

3. Statistical Analysis

The PQStat software (version 1.6.6, PQStat, Poznań, Poland) was used for statistical analysis. The normality of distribution for continuous variables was confirmed with the

Shapiro–Wilk test. Categorical data were expressed as counts and percentages, while continuous data were presented as mean (SD). The comparison between groups of patients qualified for individual treatment strategies was performed using the chi-square test, and the statistical analysis was executed using 1-way analysis of variance (ANOVA). To compare the outcomes for all strategies, the hazard ratios (HRs) with 95% confidence intervals (95% CI) were calculated. Time to event analysis was performed using Kaplan-Meier curves. All p values (p) were given to at least 2-sided, and p values lower than 0.05 were considered statistically significant.

4. Results

4.1. Study Population and Baseline Characteristics

From January 2016 to December 2019, 176 MHT meetings were held and total of 1286 patients with severe CAD (3-VD or/and LM disease) meeting inclusion and exclusion criteria with completely implemented MHT decisions (963 (74.9%) male, age (years, mean (SD)) = 69.0 (10.0), BMI (Body Mass Index) (kg/m^2 (kilogram per square meter), mean (SD)) = 27.9 (3.5), EuroSCORE II (European System for Cardiac Operative Risk Evaluation II) (%, mean (SD)) = 5.5 (1.7), STS (Society of Thoracic Surgeons) score (%, mean (SD)) = 3.5 (1.2) and given co-morbidities) were followed up. Nearly 41% of participants presented with myocardial infarction with or without ST-segment elevation or unstable angina, 3.4% with cardiogenic shock, while the rest had chronic symptoms of CAD. Regarding statistically significant differences between CABG, PCI, and OMT groups, patients who qualified for OMT were significantly older and more frail. They presented more often with HF, severe left ventricle (LV) dysfunction (EF < 30%), increased left ventricle end-diastolic diameter (LVEDD) and NYHA III-IV class, were often burdened with atrial fibrillation (AF), CKD, anemia, severe PH, cancer, and with the highest perioperative risk of intervention assessed both by EuroSCORE II and STS than those with implemented CABG or PCI ($p < 0.01$). For interventional strategies, the mean delay time from MHT decision to implementation was significantly longer for CABG-patients than in PCI-group (mean (SD): 8.4 (1.3) vs. 4.2 (0.9) days, respectively; $p < 0.01$). Regarding angiographic parameters, participants qualified for CABG and PCI had more coronary lesions affected and often LM stenosis than those from the OMT group ($p < 0.01$). Complete revascularization was achieved more frequently in CABG-group than in PCI-patients (65.4% vs. 58.5%; $p < 0.01$). Baseline clinical characteristics (overall and by groups) in detail are presented in Table 1.

Table 1. Baseline clinical characteristics.

Baseline Characteristic	Overall (1286)	CABG (356)	PCI (679)	OMT (251)	p-Value
Age, years; mean (SD)	69.0 (10.0)	66.9 (9.2)	68.8 (10.1)	72.5 (9.9)	<0.01
Gender, male (%)	963 (74.9)	289 (81.2)	495 (72.9)	179 (71.3)	<0.01
BMI, kg/m^2; mean (SD)	27.9 (3.5)	27.9 (3.3)	28.2 (3.7)	27.2 (3.0)	<0.01
Clinical Presentation					
ACS, n (%)	526 (40.9)	152 (42.7)	285 (42.0)	89 (35.5)	0.14
Cardiogenic shock, n (%)	44 (3.4)	4 (1.1)	29 (4.3)	11 (4.4)	0.02
Heart Failure, n (%)	965 (75.0)	236 (66.3)	498 (73.3)	231 (92.0)	<0.01
LV dysfunction (EF < 50%), n (%)	1067 (83.0)	289 (81.2)	567 (83.5)	211 (84.1)	0.56
LV dysfunction (EF < 30%), n (%)	336 (26.1)	46 (12.9)	147 (21.6)	143 (57.0)	<0.01
LVEDD, cm (SD)	5.8 (1.0)	5.5 (0.9)	5.8 (1.0)	6.2 (1.0)	<0.01

NYHA class III-IV, *n* (%)	441 (34.3)	95 (26.7)	217 (32.0)	129 (51.4)	<0.01
CCS class III-IV, *n* (%)	518 (40.3)	165 (46.3)	266 (39.2)	87 (34.7)	0.01
Diabetes, *n* (%)	393 (30.6)	98 (27.5)	219 (32.3)	76 (30.3)	0.29
Requiring insulin, *n* (%)	131 (10.2)	29 (8.1)	76 (11.2)	26 (10.4)	0.30
Hypertension, *n* (%)	1068 (83.0)	291 (81.7)	577 (85.0)	200 (79.7)	0.12
Previous stroke/TIA, *n* (%)	112 (8.7)	26 (7.3)	60 (8.8)	26 (10.4)	0.42
Atrial fibrillation, *n* (%)	351 (27.3)	67 (18.8)	189 (27.8)	95 (37.8)	<0.01
Previous MI, *n* (%)	615 (47.8)	189 (53.1)	319 (47.0)	107 (42.6)	0.03
Previous PCI, *n* (%)	382 (29.7)	91 (25.6)	217 (32.0)	74 (29.5)	0.10
Previous CABG, *n* (%)	115 (8.9)	20 (5.6)	71 (10.5)	24 (9.6)	0.03
PAD, *n* (%)	78 (6.1)	14 (3.9)	49 (7.2)	15 (6.0)	0.11
Carotid AD, *n* (%)	133 (10.3)	34 (9.6)	77 (11.3)	22 (8.8)	0.44
CKD, *n* (%)	463 (36.0)	66 (18.5)	204 (30.0)	193 (76.9)	<0.01
Anaemia, *n* (%)	428 (33.3)	89 (25.0)	182 (26.8)	157 (62.5)	<0.01
Dyslipidemia, *n* (%)	1028 (79.9)	284 (79.8)	556 (81.9)	188 (74.9)	0.06
COPD, *n* (%)	129 (10.0)	29 (8.1)	70 (10.3)	30 (12.0)	0.29
Severe PH, *n* (%)	125 (9.7)	17 (4.8)	73 (10.8)	35 (13.9)	<0.01
Cancer, *n* (%)	215 (16.72)	22 (6.2)	104 (15.3)	89 (35.5)	<0.01
Current smoking, *n* (%)	234 (18.2)	65 (18.3)	132 (19.4)	37 (14.7)	0.26
Frailty, *n* (%)	261 (20.3)	9 (2.5)	89 (13.1)	163 (64.9)	<0.01
Angiographic Characteristics					
No. of lesions, mean (SD)	4.2 (1.5)	4.2 (1.4)	4.3 (1.5)	3.8 (1.4)	<0.01
LM disease (LM stenosis ≥ 50%), *n* (%)	313 (24.3)	109 (30.6)	158 (23.3)	46 (18,3)	<0.01
Bifurcation, *n* (%)	927 (72.1)	261 (73.3)	491 (72.3)	175 (69.7)	0.61
CTO, *n* (%)	305 (23.7)	77 (21.6)	164 (24.2)	64 (25.5)	0.50
SYNTAX score; mean (SD)	30.2 (6.3)	31.1 (5.9)	29.6 (6.5)	30.6 (6.1)	<0.01
Complete revascularization, *n* (%)	630/1035 (60.9)	233 (65.4)	397 (58.5)	-	0.03
EuroSCORE II, %; mean (SD)	5.5 (1.7)	3.9 (1.1)	6.0 (1.4)	6.5 (1.5)	<0.01
STS score, %; mean (SD)	3.5 (1.2)	2.5 (0.8)	3.9 (1.0)	4.2 (1.1)	<0.01
Time to procedure, days (SD)	5.7 (2.3)	8.4 (1.3)	4.2 (0.9)	-	<0.01

CABG—coronary artery bypass grafting, PCI—percutaneous coronary intervention, OMT—optimal medical therapy, BMI—body mass index, ACS—acute coronary syndrome, LV—left ventricle, LVEDD—left ventricle end-diastolic diameter, Canadian Cardiovascular Society CCS—Canadian Cardiovascular Society, NYHA—New York Heart Association, TIA—transient ischemic attack, MI—myocardial infarction, PAD—peripheral artery disease, AD—artery disease, CKD—chronic kidney disease, COPD—chronic obstructive pulmonary disease, PH—pulmonary hypertension, LM—left main, CTO—chronic total occlusion, SYNTAX—Synergy between PCI with Taxus and Cardiac Surgery, EuroSCORE II—European System for Cardiac Operative Risk Evaluation II, STS—Society of Thoracic Surgeons score.

4.2. Medications at Discharge

Optimal medical therapy was administrated for all participants, most frequently using aspirin, $P2Y_{12}$ inhibitor, statin, ACE (Angiotensin-Converting Enzyme) inhibitor, and beta-blocker in the PCI-group, VKA (Vitamin K Antagonist) in the CABG-group, and NOAC (Novel Oral Anti Coagulants) loop diuretic, aldosterone antagonist, and amiodarone in the OMT-group ($p < 0.05$). The discharged medications are presented in Table 2.

Table 2. Cardiac-related medications given at discharge.

Medication at Discharge, *n* (%)	Overall (1233)	CABG (339)	PCI (654)	OMT (240)	*p*-Value
Aspirin	1150 (93.3)	302 (89.1)	631 (96.5)	217 (90.4)	<0.01
$P2Y_{12}$ inhibitors	740 (60.0)	71 (20.9)	635 (97.1)	34 (14.2)	<0.01
Vitamin K antagonist (VKA)	68 (5.5)	29 (8.6)	23 (3.5)	16 (6.7)	<0.01
Novel oral anticoagulants (NOAC)	335 (27.2)	52 (15.3)	186 (28.4)	97 (40.4)	<0.01
Statin	1135 (92.1)	294 (86.7)	628 (96.0)	213 (88.8)	<0.01
ACE inhibitor	853 (69.2)	206 (60.8)	479 (73.2)	168 (70.0)	<0.01
Angiotensin II-receptor antagonist	278 (22.5)	85 (25.1)	144 (22.0)	49 (20.4)	0.37
Beta-blocker	952 (77.2)	270 (79.6)	528 (80.7)	154 (64.2)	<0.01
Calcium-channel blocker	294 (23.8)	71 (20.9)	157 (24.0)	66 (27.5)	0.19
Loop diuretic	875 (71.0)	228 (67.3)	434 (66.4)	213 (88.8)	<0.01
Aldosterone antagonist	396 (32.1)	43 (12.7)	187 (28.6)	166 (69.2)	<0.01
Amiodarone	75 (6.1)	27 (8.0)	28 (4.3)	20 (8.3)	0.02

CABG—coronary artery bypass grafting, PCI—percutaneous coronary intervention, OMT—optimal medical therapy, $P2Y_{12}$ inhibitors—clopidogrel, prasugrel, ticagrelor, ACE—angiotensin-converting enzyme.

4.3. Endpoints

The occurrence of the primary endpoint was statistically the most frequent in the OMT group (154 patients (61.4%)), while in CABG and PCI groups—110 (30.9%) and 302 (44.5%) patients, respectively ($p < 0.05$). Excluding in-hospital mortality, CABG and PCI were significantly superior to OMT for other secondary endpoints ($p < 0.05$). Considering the endpoints for interventional strategies only, CABG was associated with reduced risk of MACCE and repeat revascularization, while the superiority of PCI for stroke and disabling stroke was observed ($p < 0.05$). However, no statistically significant differences between CABG and PCI concerning the occurrence of the composite of all-cause mortality, stroke, or MI, and all-cause mortality, CV death, MI and graft occlusion, or stent thrombosis were observed ($p > 0.05$). Postprocedural hospital stay was significantly longer for CABG-patients than in PCI-group (mean (SD): (9.9 (1.4) vs. 4.3 (0.7) days, respectively; $p < 0.01$). The endpoints comparing CABG, PCI, and OMT are detailed in Table 3. The Kaplan-Meier curves comparing all strategies for primary and secondary endpoints are presented in Figure 2.

Table 3. Primary and secondary endpoints.

Endpoints, *n* (%)	CABG (356)	PCI (679)	OMT (251)	*p* Value Overall	CABG vs. PCI HR [95% CI]; *p*	CABG vs. OMT HR [95% CI]; *p*	PCI vs. OMT HR [95% CI]; *p*
Primary Endpoint—MACCE	110 (30.9)	302 (44.5)	154 (61.4)	<0.01	<0.01	<0.01	<0.01
Secondary Endpoints							
All-cause mortality, stroke, or MI	69 (19.4)	136 (20.0)	139 (55.4)	<0.01	0.80	<0.01	<0.01
All-cause mortality	32 (9.0)	75 (11.0)	72 (28.7)	<0.01	0.30	<0.01	<0.01
CV death	24 (6.7)	64 (9.4)	43 (17.1)	<0.01	0.14	<0.01	<0.01
In-hospital mortality	17 (4.8)	25 (3.7)	11 (4.4)	0.68	0.40	0.82	0.62
MI	29 (8.1)	78 (11.5)	48 (19.1)	<0.01	0.09	<0.01	<0.01
Stroke	21 (5.9)	14 (2.1)	24 (9.6)	<0.01	<0.01	0.09	<0.01
Disabling stroke	13 (3.7)	6 (0.9)	15 (6.0)	<0.01	<0.01	0.18	<0.01
Repeat/need for revascularization	38 (10.7)	165 (24.3)	19 (7.6)	<0.01	<0.01	0.20	<0.01
CABG	9 (2.5)	17 (2.5)	0 (0.0)	0.04	0.98	0.01	0.01
PCI	29 (8.1)	148 (21.8)	19 (7.6)	<0.01	<0.01	0.80	<0.01
Graft occlusion or stent thrombosis	20 (5.6)	40 (5.9)			0.86		
Acute (at ≤1 day)	2 (0.6)	5 (0.7)			0.75		
Subacute (within 2–30 days)	3 (0.8)	13 (1.9)			0.18		
Late (within 31–365 days)	9 (2.5)	8 (1.2)			0.10		
Very late (≥366 days)	6 (1.7)	14 (2.1)			0.68		
Postprocedural hospital stay, days; mean (SD)	9.9 (1.4)	4.3 (0.7)			<0.01		

MACCE—MACCE (death from any cause, stroke, myocardial infarction, or repeat/need for revascularization), CABG—coronary artery bypass grafting, PCI—percutaneous coronary intervention, OMT—optimal medical therapy, CV—cardiovascular, MI—myocardial infarction.

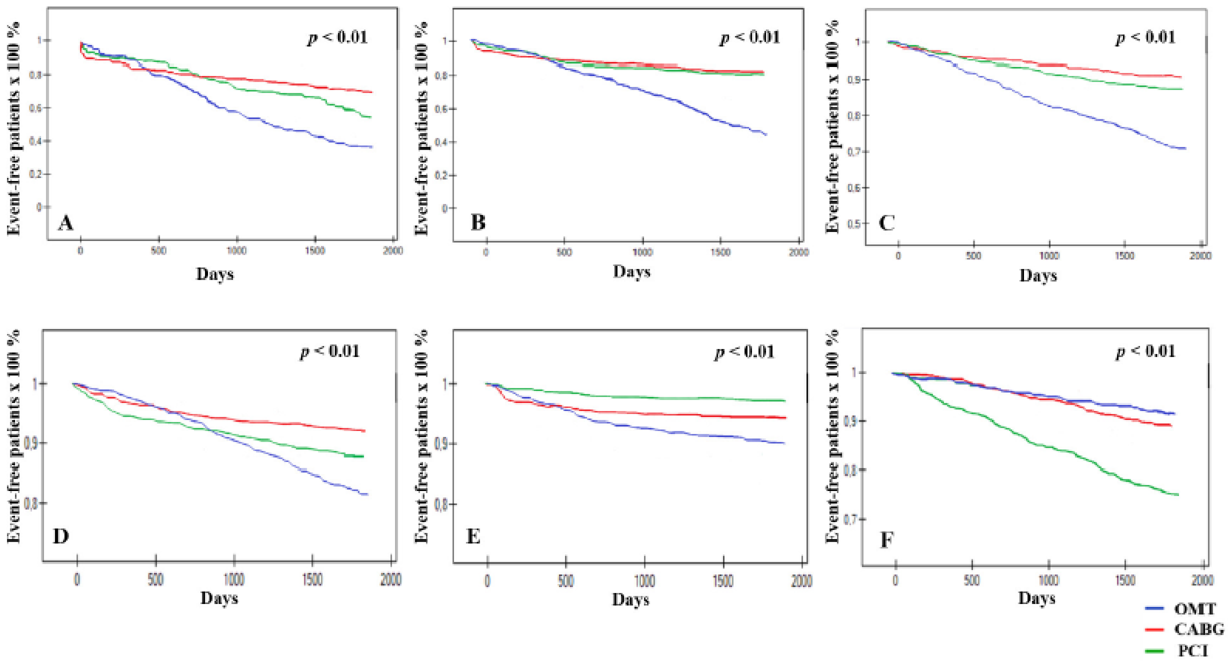

Figure 2. The Kaplan-Meier curves for endpoints. (**A**)—MACCE (death from any cause, stroke, myocardial infarction, or repeat/need for revascularization), (**B**)—all-cause mortality, stroke or myocardial infarction (MI), (**C**)—all-cause mortality, (**D**)—MI, (**E**)—stroke, (**F**)—repeat/need for revascularization.

4.4. Quality of Life

General health status assessed before implementing MHT decisions (PCS, MCS, and total) did not statistically differ between treatment strategies ($p > 0.05$). At the EOF, the results of PCS, MCS, and the total for all living participants were significantly the lowest for CABG, then for PCI, and highest for OMT-group ($p < 0.05$) as detailed in Table 4. According to the Polish version of the questionnaire, with a maximum of 103 points for PCS and 68 points for MCS (171 points total), the highest point value means the lowest quality of life assessment, while the lowest point value indicates the highest level of quality of life.

Table 4. The quality of life before and after multidisciplinary Heart Team (MHT) decisions implementation.

Component	CABG (356/324)	PCI (679/604)	OMT (251/179)	*p*-Value
Physical Component Summary (PCS)				
Before CABG, PCI, MHT disscusion; mean (SD)	71.1 (18.6)	73.2 (18.4)	73.8 (15.8)	0.12
After CABG, PCI, MHT disscusion—at the end of follow up; mean (SD)	62.0 (17.0)	65.7 (14.3)	75.0 (15.9)	<0.01
Mental Component Summary (MCS)				
Before CABG, PCI, MHT disscusion; mean (SD)	51.6 (9.4)	52.0 (9.4)	52.5 (9.0)	0.53
After CABG, PCI, MHT disscusion—at the end of follow up; mean (SD)	43.3 (9.4)	44.9 (9.7)	53.3 (8.9)	<0.01
Total				
Before CABG, PCI, MHT disscusion; mean (SD)	122.8 (20.2)	125.2 (20.6)	126.3 (18.7)	0.07
After CABG, PCI, MHT disscusio—at the end of follow up; mean (SD)	105.3 (18.8)	110.7 (16.8)	128.3 (19.5)	<0.01

CABG—coronary artery bypass grafting, PCI—percutaneous coronary intervention, OMT—optimal medical therapy, MHT—multidisciplinary Heart Team.

4.5. Logistic Regression Analysis

Moreover, to determine the factors (from baseline clinical characteristics, echocardiographic, and angiographic parameters) independently related to increased occurrence of primary endpoint and decreased survival rate, we have performed multivariable, multinominal logistic regression analysis involving the overall cohort of patients with severe CAD following MHT discussion and decisions implementation.

Our analysis revealed that (independent, of final treatment strategies—CABG + OMT, PCI + OMT, OMT) age, cardiogenic shock on admission, LV dysfunction (EF < 30 %), NYHA class III-IV, diabetes requiring insulin, PAD, CKD, anaemia, COPD, severe PH, cancer, frailty, LM disease, CTO and EuroSCORE II, were independent factors associated with increased occurrence of primary endpoint in long term follow-up (p = 0.02, <0.01, <0.01, 0.03, 0.04, 0.02, <0.01, <0.01, <0.01, <0.01, <0.01, <0.01, 0.03, 0.01, <0.01, respectively).

Independent factors negatively associated with 3-year survival (mean follow-up (SD) = 37 (14) months) were the same as for primary endpoint, but also male gender, previous stroke/TIA and carotid AD (p = 0.04, <0.01, 0.02, respectively).

5. Discussion

In this retrospective study examining patients with severe CAD who underwent MHT evaluation and were then treated in accordance with MHT decisions, the main findings were as follows: (1) patients presented during MHT consultations had a mean age of 69, high EuroSCORE II, STS and SYNTAX score, nearly one-third had diabetes and more than 25% had severe LV dysfunction; (2) patients qualified for OMT were significantly older, much burdened with comorbidities and frailty, with increased LVEDD and higher risk of intervention (assessed both by EuroSCORE II and STS score) compared with those qualified for CABG or PCI; (3) participants had increased odds of receiving CABG if they were younger, male and with LM disease, while less often had HF, severe symptoms of HF (NYHA III-IV), or severe LV dysfunction (EF < 30%), history of AF, previous MI or CABG, CKD, anaemia, severe PH, cancer, or more often presented with cardiogenic shock and with the most severe symptoms of CAD—clinical (CCS III-IV) and angiographic (SYNTAX score); (4) those with the highest BMI and the largest number of lesions affected had received PCI; (5) excluding in-hospital mortality, the occurrence of primary and secondary endpoints were significantly increased in OMT-group; (6) comparing interventional strategies—rates of MACCE were significantly higher in the PCI-group, in large part because of an increased rate of repeat revascularization (24.3% vs. 10.7%; $p < 0.05$); (7) although stroke and disabling stroke were more frequent in CABG-patients and PCI-patients had higher rates of repeat revascularization, no difference in hard clinical endpoints as composite of all-cause mortality, stroke, or MI, and all-cause mortality, in-hospital mortality, CV death, MI, graft occlusion, or stent thrombosis were observed.

Although risk assessment appears to be a decisive component in the relevant preprocedural selection of the optimal management strategy for patients with severe CAD, there are limitations to the scoring systems used to estimate the risk of adverse outcomes, and many other conditions should be evaluated to properly choose the best treatment option. Hence, the decision cannot be attributed to individuals but to a group of specialists. In our self-experience, the MHT approach was suitable and effective for individual-specific decision-making in patients with severe CAD. One of the main challenging problems for MHT is the management of critically ill or hemodynamically unstable patients who need an urgent decision. That is why only 3.4% of participants we discussed had presented with cardiogenic shock. Which is worth noting, more than a third of patients (40.9%) were admitted due to unstable angina or MI and—despite the fact they need urgent management—were carefully discussed by MHT. Hence, we supposed that a majority of the medical community believe that MHT will provide the most effective treatment for their patients. We observed that patients qualified for OMT were the oldest: we think there are basically two reasons for this phenomenon—firstly, in old age, people are afraid of invasive strategy and prefer pills; secondly—for elderly (mainly due to high risk)—cardiologists are more careful about intervention. This finding may reflect that we pay attention to many factors not included in commonly used risk scales—for example frailty, poor mobility, and patient preferences, which give our observations and results real-life clinical value. Considering interventional treatment, for younger patients but with significant LM disease, MHT tended to choose CABG, while for those with severe HF, LV dysfunction, and with more comorbidities, we prefer PCI. These results reflect recommendations and general perception of the medical community, which support better long-term outcomes associated with CABG and greater safety of PCI for highly burdened patients. Interestingly, we did not observe a trend in choosing a treatment strategy for diabetic patients, and even statistically insignificant, but a greater percentage of these participants received PCI or OMT. This is somewhat different from the current guidelines for myocardial revascularization, in which for patients with LM disease or 3-VD and high SYNTAX score, CABG is recommended strategy [22]. The discrepancy may be explained by the fact that the cohort of patients consulted by our internal MHT is not representative of the overall population of CAD individuals, and we attach great importance to the preferences of patients who are often afraid of open surgery.

Through our study, we would highlight the need for research to determine the MHT definition and range of functioning by which it can be assessed to advance our comprehension of the optimal care model for CAD patients. The development of new therapeutic options and now and then changes in evidence-based cardiology have added to the complexity of medical decision-making. Importantly, since we have started our research, there have been major technical and procedural advancements in interventional cardiology. These include physiology-based revascularization methods, such as the hybrid use of instantaneous wave-free ratio (iFR) and fractional flow reserve (FFR), newer generations drug-eluting stents, intravascular ultrasound (IVUS)-guided optimization of stent deployment, improved contemporary chronic total occlusion (CTO) revascularization techniques, and improved guideline-directed medical therapy. Therefore, in each subsequent year of the study, we referred more and more patients to PCI.

Considering endpoints for all strategies, the OMT group had demonstrated the highest frequency of most MACCE (excluding in-hospital mortality and repeat/need for revascularization), mostly due to old age, multiple comorbidities, and frailty. For interventional strategies only, beyond similar outcomes (for in-hospital mortality, all-cause mortality, CV death, MI and graft occlusion or stent thrombosis)—CABG was associated with a lower occurrence of MACCE and reduced need for repeat revascularization, while the superiority of PCI over CABG for stroke and disabling stroke was observed. Although our study is only single-center and retrospective, its outcomes are consistent with an important multi-center randomized trial for CAD-patients (SYNTAX) [12], in which rates of MACCE at 12 months were significantly higher for the PCI group (17.8%, vs. 12.4% for CABG; $p = 0.002$), mainly due to an increased rate of repeat revascularization (13.5% vs. 5.9%, $p < 0.001$) and at 1 year, the rates of death and MI were similar between PCI and CABG, while the incidence of stroke was significantly frequent in CABG group.

In our opinion, only the cooperation of MHT (where the risk assessment is only a component) provides complex decision-making with an appraisal of factors not routinely included in risk algorithms, which is the best to reflect the circumstances of real-world clinical practice. More importantly, more clinical trials comparing treatment options for CAD patients mainly focus on interventional strategy and neglect the long-term outcomes and quality of life for patients enrolled in conservative management after MHT evaluation.

It seems to be essential to discuss some important studies in which MHT was involved in the selection of appropriate CAD patients and the multifactorial decision-making process. The very first such study, with the MHT conception touched upon, was SYNTAX (outcomes presented above) [12], in which each clinical case and angiogram was reviewed by a team consisting of an interventionist and a surgeon. After a consensus agreement, the decision for which procedure or procedures the patient may be eligible for was made.

Subsequently, the first review article by Head SJ et al. raised the issue of adjusting the MHT concept with available diagnostic evidence, patient preferences, local expertise, and constantly changing recommendations to provide the most beneficial outcomes for CAD patients [13]. After that, in 2014, 5-year outcomes of patients with 3-VD ($n = 1095$) treated with CABG or PCI using the first-generation paclitaxel-eluting stents from SYNTAX trial were revealed, resulting in significantly lower rates of death, MI, and repeat revascularization in the CABG cohort, while stroke rates were similar [14]. Furthermore, Bonzel T et al., and then Abdulrahman M, et al. stressed the impact of the structured MHT approach and the hierarchy of the participating physicians for clinical decision-making associated with improved outcomes [15,16]. In another study by Collet C et al., separate MHTs composed of an interventional cardiologist, a cardiac surgeon, and a radiologist were randomized to assess the CAD with either coronary computed tomography angiography (CTA) or conventional angiography in 223 patients with de novo LM stenosis or 3-VD. MHT compliance in assessing patients' qualification for PCI or CABG procedures (the primary endpoint) was very high and amounted to approximately 93%. Cohen's Kappa coefficient was 0.82, indicating almost complete agreement between the two teams. Additional data from the non-invasive assessment of FFR CTA (a secondary endpoint) changed the decision of MHT in 14 patients (7%), of which in 13 patients it meant a requalification from surgery to percutaneous treatment [17].

Afterward, some observational studies evaluated the MHT approach for CAD patients in single-center experiences [18–20]. In the study by Patterson T et al. from 2012 to 2013, 51 MHT meetings were held, and a total of 366 cases were discussed providing MHT recommendation and outcome of CABG + OMT, PCI + OMT, and OMT alone in 27.9%, 34.7%, and 37.4% of cases, respectively. The 3-year survival rate was 60.8%, 84.3%, and

90.2% in the OMT, OMT + PCI, and 90.2% in the OMT + CABG cohorts, respectively. Medical therapy was associated with a 4.5-fold increased risk of mortality compared with CABG and PCI (HR: 4.588; 95% CI: 2.333–9.021; $p < 0.001$) [18]. Dominiques CT et al. presented assigning nearly 1000 patients to CABG, PCI, OMT, or additional diagnostic methods depending on the number of affected coronary vessels, MHT decisions, and patients' preferences, emphasizing that the final MHT recommendation was largely in accordance with clinical guidelines [19]. In another research, out of the 166 patients discussed at MHT meetings, 79 (47.6%) underwent PCI, 49 (29.5%) underwent CABG, 1 (0.6%) underwent hybrid revascularization, and 34 (20.5%) were treated with OMT only. Among 129 patients who underwent revascularization (PCI or CABG), the in-hospital and 30-day mortality was 3.9% and 4.8%, respectively, while there were no trends in recommendations for CABG, PCI, or OMT by SYNTAX score tertiles [20].

Very recently, the SYNTAX II strategy of incorporating both clinical and anatomical variables into MHT decisions to guide myocardial revascularization led to better 5-year clinical outcomes in comparison with the SYNTAX trial, which evaluated anatomic factors only [21]. A total of 454 patients were included and compared with 315 patients from the pre-defined SYNTAX PCI group and 334 patients from the pre-defined SYNTAX CABG cohort. At 5 years, MACCE (composite of all-cause death, stroke, any MI, and any revascularization) occurred in 21.5% of SYNTAX II patients, which was significantly lower than the 36.4% MACCE rate in the SYNTAX PCI group (HR: 0.54; 95% CI: 0.41–0.71; $p < 0.001$). All MACCE components, except stroke, were significantly lower in SYNTAX II PCI patients [21]. This study proves the relevance of MHT management—taking into account that clinical parameters through decision-shared making resulted in better clinical outcomes for SYNTAX II patients than a matched PCI group from SYNTAX.

There are several methodological strengths in this study that reinforce the validity of the obtained results: all-comer nature, retrospective enrolment, systematic and meticulous patient assessment, complete mean 37-months clinical follow-up, assessment of the quality of life, and the use of standardized definitions and endpoints for clinical outcomes support the universal value of these data. Moreover, quite a large group of patients (as regards the conditions of single-center study) and a long follow-up is sufficient to determine with high probability that decisions of our MHT are adequate and consistent with clinical practice. Furthermore, properly selected endpoints, clearly reflecting the most common and serious complications of CAD-interventional treatment, prove the translatability of the obtained results on the proper functioning of MHT.

6. Conclusions

In our study, we presented how the MHT approach and decisions affect the prognosis and quality of life of patients with severe CAD, demonstrating that those qualified by our internal MHT for interventional strategy achieved greater benefits in both endpoints and long-term quality of life as compared to pharmacological treatment only. It should be especially emphasized that for CAD patients, choosing the best treatment method should never be individual. The results of this study require further confirmation in longer follow-up or multi-center studies and registers, but our initial findings may establish a cornerstone for the future providing establishment of MHT role both in clinical practice and guidelines for CAD management.

Limitations

This study should be interpreted given the following limitations. The main one is its retrospective, non-randomized character, and single-center design. Above that, the decision-making process must be assigned to our individual MHT cooperation and cannot be considered a general one. Additionally, proper and regular use of drugs by patients often remains a matter of trust; hence it is difficult to determine the credibility of the endpoints in the OMT group. Moreover, patients with non-implemented decisions were not included in the final analysis, so we do not have their follow-up data. Participants were not matched; hence the comparison of groups should be considered with caution. Individuals qualified for interventional strategies differ significantly in some clinical parameters. Thus, the obtained outcomes cannot contribute to formulating far-reaching and unquestionable conclusions.

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8.4. An Individualized Approach of Multidisciplinary Heart Team for Myocardial Revascularization and Valvular Heart Disease—State of Art.

Journal of *Personalized Medicine*

MDPI

Review

An Individualized Approach of Multidisciplinary Heart Team for Myocardial Revascularization and Valvular Heart Disease—State of Art

Szymon Jonik [1,*], Michał Marchel [1], Zenon Huczek [1], Janusz Kochman [1], Radosław Wilimski [2], Mariusz Kuśmierczyk [2], Marcin Grabowski [1], Grzegorz Opolski [1] and Tomasz Mazurek [1,†]

1 1st Department of Cardiology, Medical University of Warsaw, Banacha 1a Str., 01-267 Warsaw, Poland; michal.marchel@gmail.com (M.M.); zhuczek@wp.pl (Z.H.); jkochman@tlen.pl (J.K.); marcin.grabowski@wum.edu.pl (M.G.); grzegorz.opolski@wum.edu.pl (G.O.); tmazurek@kardia.edu.pl (T.M.)

2 Department of Cardiac Surgery, Medical University of Warsaw, Banacha 1a Str., 01-267 Warsaw, Poland; rwilimski@gmail.com (R.W.); prof.kusmierczyk@gmail.com (M.K.)

* Correspondence: szymonjonik.wum@gmail.com; Tel.: +48-22-599-19-58; Fax: +48-22-599-19-57

† Senior author.

Abstract: The multidisciplinary Heart Team (HT) remains the standard of care for highly-burdened patients with coronary artery disease (CAD) and valvular heart disease (VHD) and is widely adopted in the medical community and supported by European and American guidelines. An approach of highly-experienced specialists, taking into account numerous clinical factors, risk assessment, long-term prognosis and patients preferences seems to be the most rational option for individuals with. Some studies suggest that HT management may positively impact adherence to current recommendations and encourage the incorporation of patient preferences through the use of shared-decision making. Evidence from randomized-controlled trials are scarce and we still have to satisfy with observational studies. Furthermore, we still do not know how HT should cooperate, what goals are desired and most importantly, how HT decisions affect long-term outcomes and patient's satisfaction. This review aimed to comprehensively discuss the available evidence establishing the role of HT for providing optimal care for patients with CAD and VHD. We believe that the need for research to recognize the HT definition and range of its functioning is an important issue for further exploration. Improved techniques of interventional cardiology, minimally-invasive surgeries and new drugs determine future perspectives of HT conceptualization, but also add new issues to the complexity of HT cooperation. Regardless of which direction HT has evolved, its concept should be continued and refined to improve healthcare standards.

Keywords: heart team; decision-making; coronary artery disease; mitral regurgitation; aortic stenosis; interventions

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1. Introduction

With an aging population, the increase in prevalence of atherosclerosis, coronary artery disease (CAD) and valvular heart diseases (VHD), degenerative and secondary to heart failure (HF) are expected. There is an unquestionable belief in the medical community that the standards of treatment should be incessantly improved with the use of experienced Heart Teams (HT) to provide the most satisfactory outcomes. An approach of multispecialist HTs is the most wanted to best assess the strengths and weaknesses of various treatment strategies for patients burdened with many co-morbidities. However, the HT management for "difficult" individuals is recommended in European and American guidelines both for myocardial revascularization and VHD [1–7]; this proceeding is mostly driven by expert opinion, whereas data from randomized-controlled trials (RCTs) supporting this approach is still scarce. Several studies suggest that through shared-decision making according to the guidelines, HT may improve overall outcomes. There is only a recognition, however, for real-life evidence we have to satisfy with observational studies describing outcomes of a multidisciplinary approach without a comparator.

The selection between interventional or medical treatment was originally based in the structure of HT from its first concept in the early 1980s [8,9]. We have known since then that each complex case should be discussed by at least three specialists: clinical and interventional cardiologists, and cardiac surgeons. With time and new treatment modalities, more specialists have been incorporated into HT structures and actively participated in the HT meetings depending on the complexity of the case. Moreover, there are many variables associated with the decision-making process as HT has been focused on the patient, not only selected disease treatment. Therefore, a holistic approach, risk assessment, specialists experience' and the capabilities of the centre are also important (Figure 1).

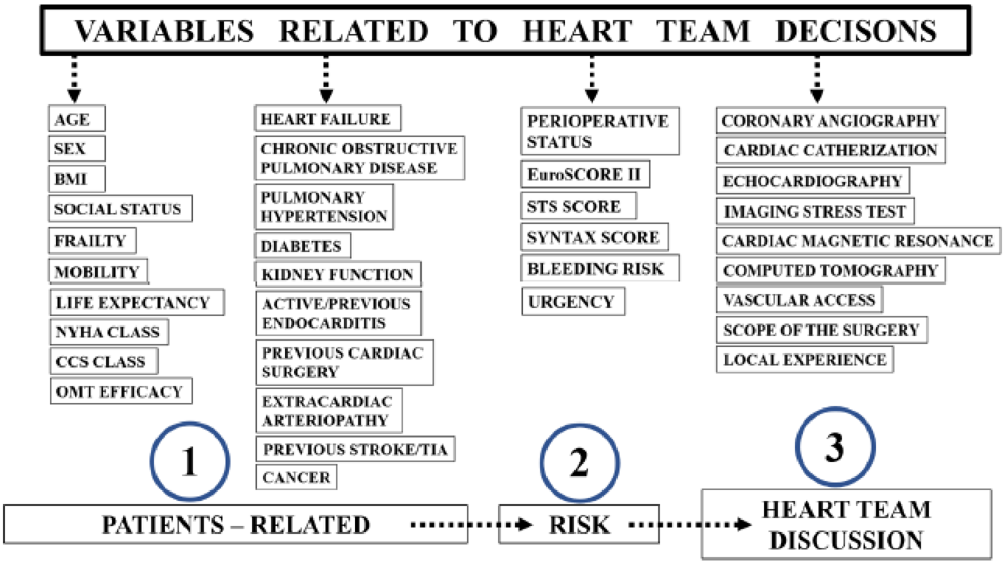

Figure 1. The variables associated with Heart Team decision-making process. NYHA—New York Heart Association, CCS—Canadian Cardiovascular Society, OMT—optimal medical therapy, EuroSCORE II—European System for Cardiac Operative Risk Evaluation, STS—Society of Thoracic Surgeons, SYNTAX—Synergy Between PCI with Taxus and Cardiac Surgery.

Nowadays, the cooperation of HT seems to be virtually impossible without an experienced echocardiographist, radiologist and other imaging specialists who can assist with determination of disease severity, scope of the surgery and its expediency and feasibility. An anaesthesiologist can assess the perioperative risk for a patient who may undergo surgery or percutaneous procedure and give insights about the safety of general anaesthesia. A critical care intensivist is needed to guide the patient in the postoperative period. Furthermore, a nephrologist could help with those situations in which dialysis is contemplated or in case of complications such as acute kidney injury (AKI). A neurologist can assess the risk of cerebrovascular incidents and recommend prior intervention of the cerebral arteries when affected. Finally, a geriatrician could be involved in establishing of frailty status and purposefulness of interventional strategy. While the psychological aspect has been found to be an important factor in cardiovascular (CV) patients, a psychologist or physical therapist could also be incorporated into the decision process. Such approaches should be requested and actively implemented into HT protocols. The graphical cooperation of HT specialists is presented in Figure 2.

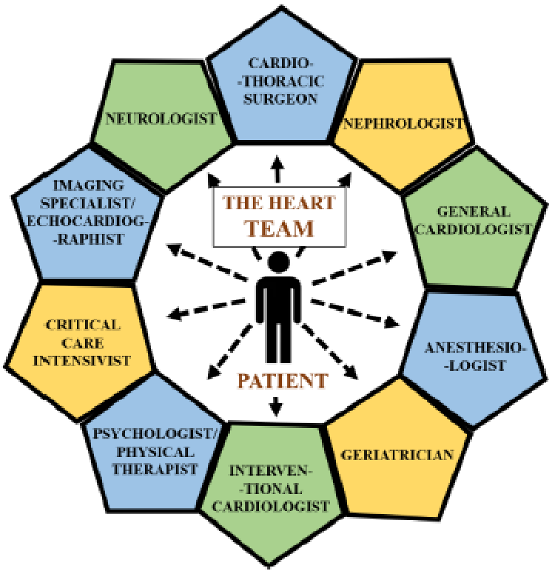

Figure 2. The HT specialists cooperation.

Below, we present, to our knowledge, the most extensive review of evidence from the literature supporting HT as desirable tool for optimal management of complex patients, providing improved outcomes and satisfactory quality of life.

2. Heart Team for Myocardial Revascularization

For many years, since CAD has been a leading problem of the modern world, ways to better diagnose and deal with this problem to improve patients' management, prognosis and quality of life are being sought. With an increasing number of percutaneous and surgical options, new drugs improving symptoms and survival and improved collaboration between cardiologists and cardiac surgeons, an idea of HT has been implemented and still plays a leading concept in the real-life care of patients with CAD (class I recommendation in European and American guidelines) [1–5]. While choice of treatment for patients with acute conditions or less complex CAD may be single-minded, for individuals with stable multivessel disease (MVD), a HT consisting of non-invasive cardiologist, interventional cardiologist, cardiac surgeon and echocardiographist is considered the most wanted for selecting the optimal method of revascularization or disqualification for intervention. In the multicentre randomized Synergy Between PCI with Taxus and Cardiac Surgery (SYNTAX) trial, in which a local interventional cardiologist and cardiac surgeon at each site prospectively evaluated eligible patients with previously untreated left main (LM) disease and/or three-vessel disease (3-VD) to perform percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), an approach of HT for MVD patients was for the first time truly incorporated. The rates of major adverse cardiac or cerebrovascular events—MACCE (death from any cause, stroke, myocardial infarction (MI), or repeat revascularization) at 12 months—were significantly higher for PCI group (17.8%, vs. 12.4% for CABG; $p = 0.002$), mainly due to an increased rate of repeat revascularization (13.5% vs. 5.9%, $p < 0.001$). The rates of death and MI were similar between PCI and CABG, while the incidence of stroke was significantly more frequent in CABG group. The researchers reported that the use of antiplatelet drugs was high in the PCI arm (with 71.1% receiving a thienopyridine at 12 months). Additionally, both the use of statin, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers and calcium channel blockers was significantly higher after the study procedure in PCI group. Highly effective dual–antiplatelet and statin therapy may prevent thromboembolic incidents; hence, the lower rates of stroke in patients undergoing PCI. However, in this trial, the outcomes of participants disqualified from interventional treatment after HT evaluation and adherence to drug use in the optimal medical therapy (OMT) group were not assessed and this fact can be a kind of drawback [10]. After that, in 2014, Head SJ, et al., presented the final results of five-year follow-up for 1095 patients with 3-VD from SYNTAX trial randomly assigned to CABG (n = 549) or PCI (n = 546). The authors concluded that CABG should remain the standard of care resulted in significantly lower rates of death, MI, and repeat revascularization in CABG cohort with the rates of stroke independent of treatment strategy [11]. Furthermore, SYNTAX III Revolution trial identified computed tomography (CT) as non-invasive alternative to conventional angiography. This study did not focus on clinical endpoints and did not randomize patients but randomized physicians and surgeons from HT to make a decision on the best treatment for complex CAD. Two individual, blinded to each other HTs, composed of an interventional cardiologist, a cardiac surgeon, and a radiologist were randomized to evaluate CAD with either coronary computed tomography angiography (CTA) or conventional angiography in 223 patients with de novo LM stenosis or 3-VD. HT compliance in the assessment of patients' qualification for PCI or CABG procedures (the primary endpoint) was very high at approximately 93%, whereas Cohen's Kappa coefficient was 0.82, which indicates almost complete agreement between the two separate teams [12]. Additional insights from SYNTAX III Revolution revealed a secondary endpoint, including the physiological component using fractional flow reserve (FFR) derived from coronary CTA (FFR_{CT}). It was demonstrated that coronary CTA evaluation with FFR_{CT} was feasible in 196 out of 223 MVD patients (87.9%). The inclusion of FFR_{CT} changed the HT treatment decision in 7% of the cases and modified the selection of vessels for revascularization in 12% as compared with a coronary CTA assessment alone. Moreover, FFR_{CT} reduced the proportion of patients with hemodynamically significant 3-VD from 92.3% to 78.8%, reclassifying them from intermediate and high to low SYNTAX score tertiles [13]. Very recently, the SYNTAX II strategy with assessment of both clinical and anatomical factors to guide myocardial revascularization was associated with improved 5-year clinical outcomes as compared with the SYNTAX trial, which evaluated anatomic variables only. For this study, 454 patients with de novo 3-VD were included and paralleled with 315 patients from the pre-defined SYNTAX PCI group and 334 patients from the pre-defined SYNTAX CABG cohort. The SYNTAX II strategy through functional assessment resulted in fewer lesions undergoing PCI, better optimization of PCI through the use of IVUS, more complete CTO revascularization, and optimal drug therapy. After 5 years, MACCE (all-cause death, any stroke, any MI, or any revascularization) occurred in 21.5% of SYNTAX II patients and was significantly lower than in the SYNTAX PCI cohort (36.4%, p <0.001). All MACCE components, except for stroke, were significantly less frequent in the SYNTAX II PCI group (p < 0.001). Also, the rate of in-stent thrombosis at 5 years was lower among SYNTAX II patients (1.4% versus 5.5%, p = 0.004).

A similar rate of MACCE in the SYNTAX II group and the SYNTAX I CABG cohort were demonstrated (21.5% versus 24.6%, p = 0.35). In addition, optimized medical therapy was a part of SYNTAX II strategy. An increased use of statins at 5 years following revascularization (83% in SYNTAX-I PCI vs. 88% in SYNTAX II; p = 0.055) may be responsible for some of the improved outcomes of patients from the SYNTAX II cohort. Furthermore, pre-procedural loading dosing of statins may be associated with meaningful decrease in periprocedural rates of MI in SYNTAX II. Although the aspirin and dual antiplatelet therapy (DAPT) recommendations were significantly more frequent in the SYNTAX II group at discharge, rates of ADP antagonist prescription at 5 years were much higher in SYNTAX-I PCI. It is likely that this fact can be explained by lower rates of repeat revascularization/MI and utilization of new generation of drug-eluting stents (DES) with less dependence of DAPT in SYNTAX II cohort. Other CV medications were similarly used among SYNTAX II and SYNTAX-I PCI [14]. Afterwards, some observational studies evaluated HT approach for CAD-patients in single-center experiences. Bonzel T, et al., reported long-term outcomes of individuals with CAD qualified by HT to PCI. Out of 11,174 catheterizations for any reason 3408 catheterizations with a new diagnosis of CAD was analyzed by specialists to select optimal treatment modality and a total number of 1527 patients with first in life PCI for CAD were followed-up. The authors concluded that the multidisciplinary approach is a powerful tool for ad hoc and conference-based decision-making with desirable outcomes.

During follow-up, CABG occurred in 15%, PCI in 37% and diagnostic catheterization in 65% of participants, while mortality of any course reached 51%. Mortality rates were similar in one-vessel disease (1-VD) and in patients matched for age and sex, but survival was significantly decreased in firstly-PCI patients with MVD [15]. Abdulrahman M, et al., presented the association between hierarchy in HT and recommendations for patients with isolated MVD. The decisions for CABG, PCI or OMT were made if the head of cardiovascular surgery (HOS) and the head of cardiology (HOC) were present, and only one of them was available or both directors were absent. When both HOC and HOS were present, only HOS was available, only HOC was available or both HOC and HOS were absent, the CABG-to-PCI ratios were 3.35, 4.88, 1.17 and 2.23, respectively.

This study demonstrated that HT decisions are not only related to current guidelines, but highly influenced by hierarchy among the members of the HT [16]. Another study assessed the long-term survival of 366 patients (74.1% with MVD, mean age 69 ± 11 years) consulted at 51 HT meetings. Depending on the baseline clinical characteristics and risk assessment, patients were qualified for CABG+OMT (n = 102), PCI+OMT (n = 127) or OMT only (n = 137). Also, the multinomial logistic regression analysis was performed to define factors associated with HT strategy, which revealed that patients had increased odds of receiving PCI if they were in cardiogenic shock or had 3-VD (not including left main stenosis (LMS)), CABG was recommended for younger and with isolated LMS, while OMT for the oldest and with diabetes mellitus (DM). 3-year survival was 60.8%, 84.3% and 90.2% in the OMT, OMT+PCI and OMT+CABG cohorts, respectively. For patients who underwent HT discussion and implementation of any revascularization strategy, no significant difference in mortality between CABG and PCI cohorts was demonstrated [17]. In 2019, Dominiques, et al., presented HT management for nearly 1000 patients with CAD, 69.4%, simple CAD and 30.6% for MVD qualified after careful HT evaluation to CABG, PCI, OMT or additional diagnostic methods depending on the number of affected coronary vessels, HT decisions and patients' preferences and followed with median (interquartile range (IQR)) time of 4.6 (4.2–5.0) years.

The authors reported no association between proximal left anterior descending (LAD) involvement and all-cause death for patients with 1-VD or 2-VD (16.4% vs. 15.7% for non-proximal LAD, p = 0.70), while for individuals with complex CAD the overall mortality was significantly increased in LMS with 2-VD or 3-VD (26.9%), p = 0.019 [18]. Young, et al., reported prospectively evaluated data of 166 high-risk patients with CAD qualified to CABG (n = 49), PCI (n = 79), OMT (n = 34) or hybrid therapy (n = 1) following HT decisions. The median (IQR) number of physicians per HT council was 6 (5–8). With increasing Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM: low, intermediate, high) operative risk, CABG was performed less often and OMT was recommended increasingly, while no trends in HT decisions for CABG, PCI or OMT by SYNTAX score tertiles were observed. Among 129 patients who underwent revascularization (CABG or PCI) in-hospital and 30-days mortality was 3.9% and 4.8%, respectively, while the 30-day unplanned rehospitalization rate was 16.4%, 22.4% and 17.6% for PCI, CABG and OMT-patients, respectively [19]. Another study compared HT decisions and delay to revascularization for MVD-patients from 2 groups: evaluating by HT (93) and control group (93) matched according to clinical and angiographic characteristics. No significant differences in CV risk, left ventricular (LV) dysfunction, STS and SYNTAX scores between these two groups were observed. After HT discussion, the percentage of patients qualified to CABG resulted in 63% and was significantly higher than in control group −23% ($p < 0.01$). HT management led to a significant delay to PCI, while delay to CABG was not affected [20]. Tsang MB, et al., reported very interesting results from a study of 234 patients with MVD comparing the treatment originally implemented by interventional cardiologists (2012–2014) with recommendations proposed by members of 8 blinded HTs (2017–2018). Between the original decisions of the interventional cardiologists and the results of the HT consultations, a different decisions occurred in nearly one-third of the cases. HT members indicated statistically insignificant, but numeric bias toward the procedure of their specialty.

Overall, as the choice of the treatment strategy is regarding, there were no statistically significant differences between interventional cardiologists and HT members for CABG ($p = 0.62$) or PCI ($p = 0.15$), while OMT was less frequently recommended originally by interventional cardiologist than by the HT members ($p = 0.04$). ([21]; and comment—[22]). We also served our internal single-centre experience with mean (standard deviation (SD)) follow-up of 37 (14) months for 1286 participants with severe CAD (3-VD and/or LM disease) and fully implemented HT decisions (OMT, CABG or PCI for 251, 356 and 679 patients, respectively). The ratio of primary endpoint—MACCE (overall death, stroke, MI, or repeat/need for revascularization) was significantly increased in OMT-group as compared with CABG or PCI ($p < 0.05$), while considering interventional strategies only—CABG was associated with reduced rates of MACCE and repeat revascularization, while the superiority of PCI for stroke and disabling stroke was observed ($p < 0.05$).

The general health status assessed at the end of follow-up was significantly more satisfactory for patients who underwent revascularization than in OMT-group ($p < 0.05$) [23]. Current evidence summarizing the role of HT for treating patients with CAD is presented in Table 1.

Table 1. Heart Team for myocardial revascularization.

Study Type	Clinical Characteristics	Results	Ref. No.
prospective, randomized	1800 patients with 3-VD or/and LMS: CABG—897, PCI—903 Follow-up: 12 months	• Rates of primary—MACCE (overall mortality, stroke, MI, repeat revascularization) at 12 months were significantly higher in the PCI group (17.8%, vs. 12.4% for CABG) mostly due to an increased rate of repeat revascularization (13.5% vs. 5.9% for CABG). • At 12 months, the rates of death and MI were similar between the two groups, while rates of stroke were significantly higher in CABG-patients (2.2%, vs. 0.6% with PCI).	[10], Serruys PW, et al.
retrospective analysis of prospective, randomized trial	1095 patients with 3-VD: CABG—549, PCI—546 Follow-up: 5 years	• The rate of MACCE (overall mortality, stroke, MI, repeat revascularization) was significantly higher in PCI as compared with CABG-patients (37.5 vs. 24.2%). • PCI vs. CABG resulted in significantly higher rates of the composite of death/stroke/MI (22.0 vs. 14.0%), all-cause death (14.6 vs. 9.2%), MI (9.2 vs. 4.0%), and repeat revascularization (25.4 vs. 12.6%). • Rates of stroke were similar between groups at 5 years (3.0 vs. 3.5%).	[11], Head SJ, et al.
prospective, randomized	223 patients with de novo 3-VD or LM disease Separate HTs randomized to assess the CAD with either coronary CTA or CA.	• HT compliance in the assessment of patients' qualification for PCI or CABG procedures (the primary endpoint) was found to be very high—approximately 93%. An almost complete agreement between the two teams was demonstrated.	[12], Collet C, et al.
prospective, randomized	223 patients with 3-VD or LM disease 2 HTs to decide between CABG and PCI FFR analysis in 196 patients FFR_{CT} available for 1030 lesions	• By noninvasive evaluation with FFR_{CT}, the HT changed decisions for 7% of patients and modified the selection of vessels for revascularization in 12% in comparison with a coronary CTA assessment alone. • For individuals assessed by coronary CTA, FFR_{CT} reduced the number of cases with hemodynamically significant 3-VD from 92.3% to 78.8%.	[13], Andreini D, et al.

Table 1. *Cont.*

Study Type	Clinical Characteristics	Results	Ref. No.
prospective, nonrandomized	454 patients with de novo 3-VD without LMS compared with 315 patients from the pre-defined SYNTAX PCI group and 334 patients from the pre-defined SYNTAX CABG cohort. Follow-up: 5 years	• The SYNTAX II strategy of incorporating both clinical and anatomical variables into HT decisions to guide myocardial revascularization was associated with improved 5-year clinical outcomes as compared with the SYNTAX trial, which evaluated anatomic factors only. • At 5 years, MACCE (composite of all-cause death, stroke, any MI and any revascularization) occurred in 21.5% of SYNTAX II patients, which was significantly lower than the 36.4% MACCE rate in the SYNTAX PCI group. • MACCE outcomes at 5 years among patients in SYNTAX II and predefined patients in the SYNTAX I CABG cohort were similar.	[14], Banning AP, et al.
retrospective	3408 catheterizations with a first diagnosis of CAD 1527 patients had first PCI Follow-up: 15 years	• During follow-up of firstly PCI—patients (Kaplan–Meier analysis), CABG occurred in 15% of patients, PCI in 37% and diagnostic catheterization in 65%; mortality of any course was 51%. • Mortalities were similar in 1-VD and in a population matched for age and sex, but mortality was significantly higher in firstly-PCI patients with MVD.	[15], Bonzel T, et al.
retrospective	209 patients with isolated MVD: CABG—141, PCI—59, OMT—9 Impact of hierarchy on multidisciplinary HT recommendations.	• The hierarchy of the participating cardiologists and cardiac surgeons significantly impacts treatment strategies of a multidisciplinary HT. • This impact did not attenuate after several years of HT interactions.	[16], Abdulrahman M, et al.
prospective	366 patients with LMS, 2-VD, 3-VD or clinical equipoise: CABG—102, PCI—127, OMT—137 Follow-up: 3 years	• OMT was associated with a 4.5-fold increased risk of overall mortality compared with CABG and PCI over the 3-year period. • No significant difference in overall survival at 3 years between CABG and PCI was observed.	[17], Patterson T, et al.
retrospective	960 patients with CAD—69.4%—simple CAD, 30.6%—complex CAD Median (IQR) follow-up: 4.6 (4.2–5.0) years	• The 5-year mortality rates were: 16.4% for 1- or 2-VD (with proximal LAD), 15.7% for 1- or 2-VD (with non-proximal LAD), 17.1% for 3-VD, 3.4% for isolated LM or with 1-VD and 26.9% for LM with 2- or 3-VD.	[18], Dominigues CT, et al.
prospective	166 high-risk patients with complex CAD: CABG—49, PCI—79, OMT—34, hybrid therapy—1 Follow-up: 3 years	• Among 129 patients who underwent revascularization (CABG or PCI) in-hospital and 30-days mortality was 3.9% and 4.8%. • The 30-day unplanned rehospitalization rate was 16.4% for PCI, 22.4% for CABG and 17.6% for OMT-patients.	[19], Young MN, et al.
prospective	186 patients with MVD: 93—HT approach, 93—control group	• 63% vs. 23 % of patients were referred to CABG after HT discussion as compared with control group. • HT discussion led to a significant delay to PCI, while delay to CABG was not affected.	[20], Kezerle L, et al.
retrospective	234 patients with MVD originally treated as recommended by interventional cardiologists (2012–2014) compared with blinded HT treatment recommendations (2017–2018)	• The treatment proposed by HT showed a 30% inconsistency with the original treatment administered by the interventional cardiologists. • Different treatment was recommended by the HT for 22% of patients who received CABG, 45% of patients who received PCI and 40% of patients who received medical therapy. • HT members indicated statistically insignificant, but numeric bias toward the procedure of their specialty.	[21], Tsang MB, et al. Comment: [22], Blankenship JC, et al.

Table 1. *Cont.*

Study Type	Clinical Characteristics	Results	Ref. No.
retrospective	1286 patients with 3-VD or/and LMS: CABG—356, PCI—679, OMT—251 Mean (SD) follow-up: 37 (14) months	• In-hospital mortality did not significantly differ between treatment strategies. • CABG and PCI were found to be significantly superior to OMT for primary endpoint (MACCE—overall mortality, stroke, MI, repeat/need for revascularization) and secondary endpoints (overall mortality, CV death, stroke, disabling stroke, MI, repeat/need for revascularization). • For interventional strategies—CABG was associated with reduced rates of MACCE and repeat revascularization, while the superiority of PCI for stroke and disabling stroke was observed.	[23], Jonik S, et al.

1-VD—one-vessel disease, 2-VD—two-vessel disease, 3-VD—three-vessel disease, LMS—left main stenosis, CABG—coronary artery bypass grafting, PCI—percutaneous coronary intervention, OMT—optimal medical therapy, MACCE—major adverse cardiac and cerebrovascular events, MI—myocardial infarction, CAD—coronary artery disease, MVD—multivessel disease, CTA—computed-tomography angiogram, CA—conventional angiography, HT—Heart Team, FFR—fractional flow reserve, FFR_{CT}—fractional flow reserve form computed-tomography, IQR—interquartile range, LAD—left anterior descending, SYNTAX—Synergy Between PCI with Taxus and Cardiac Surgery, CV—cardiovascular.

3. Heart Team for Aortic Valve Stenosis

Over the years we have observed an improved level of health care and we predict a further increase in life expectancy, and the prevalence of degenerative aortic stenosis (AS) due to aging of the population is also expected. The problem is urgent as AS is the most widespread VHD in the world and still remains the most common indication for valve intervention in Europe and North America [6,7]. The surgical aortic valve replacement (SAVR) has previously been the standard of care for AS-patients, improving both symptoms and prognosis, while since 2007, the less invasive transcatheter aortic valve replacement (TAVR) has been commercially available. Currently, the state of the art for the treatment of patients with symptomatic AS includes both conventional surgery, percutaneous treatment (TAVR) and conservative approach—OMT, depending on many variables. Although many RCTs have compared outcomes of patients with high-, intermediate- and low- risk AS who were treated with SAVR or TAVR, the role of HT was poorly underlined in these studies [24–30]. Admittedly, HT was used to evaluate the baseline status of patients and determine the perioperative risk, but not as decision-making tool for selection of the optimal treatment modalities. Current recommendations for intervention in AS–patients are guided by the RCT findings and compatible with real-world HT cooperation for individual patients (many of whom not meet the RCT inclusion criteria) [6,7].

AS is a very heterogeneous condition and the most beneficial procedure should be carefully considered by the individual HT, accounting for age, life expectancy, comorbidities and frailty, anatomical and procedural characteristics, prosthetic heart valve durability, feasibility of vascular access and local experience with long-term outcomes. While waiting for an RCT assessing the efficacy of HT approach for AS-patients, we have to be content with data from observational studies only.

For the first time, Dubois, et al., demonstrated prospective management of 163 high-risk patients with AS qualified after HT evaluation to transcatheter aortic valve implantation (TAVI)—73, SAVR (35) and OMT with or without percutaneous transluminal aortic valvuloplasty (PTAV)—55 patients. The authors reported that TAVI and SAVR was found to be significantly superior to OMT/PTAV for all-cause mortality and CV death and non-significantly superior to OMT/PTAV for repeat hospitalizations for CV cause at 1 year. For interventional procedures, the combined safety endpoint (overall mortality, major stroke, life-threatening bleeding, AKI stage 3, periprocedural MI, major vascular complication or repeat procedure for valve-related dysfunction) at 30 days favored TAVI, while the combined efficacy endpoint (overall mortality after discharge, rehospitalization for CV causes and prosthetic heart-valve dysfunction) at 1 year supported AVR approach [31].

Similarly, Thyregod HGH, et al., reported very poor prognosis for patients with severe AS qualified by HT to OMT with survival rate significantly lower as compared with TAVI– and SAVR–patients when using Cox regression analysis adjusted for age and gender ($p < 0.01$). The HT proposed intervention in 93% of patients with severe AS despite high age, advanced symptoms and a high burden of co-morbidity, while those for whom HT did not propose to undergo any intervention were older, had a higher prevalence of chronic obstructive pulmonary disease (COPD), peripheral artery disease (PAD), previous MI and cerebrovascular disease. Disqualification from any procedure resulted in a very dismal prognosis in OMT-cohort with only 57 and 26% surviving to 1 and 3 years, respectively [32].

Data from the Belgian centre revealed that TAVI as carefully discussed and passed by HT translates into similar outcomes and shorter hospital stay as compared with SAVR even for higher-risk patients. Bakelants E, et al., presented the cooperation of HT in a health-economic context with limited accessibility for transcatheter procedures. For 405 prospectively observed high-risk patients with AS qualified for SAVR—98, TAVI—188 and OMT/PTAV—116, TAVI and SAVR was found to be significantly superior to OMT/PTAV for all-cause mortality and CV death at 1 year, while no differences in stroke/transient ischemic attack (TIA) and CV-rehospitalization between groups after 30 days and at 1 year were observed [33].

In a retrospective study by Rea CW, et al., 243 individuals with severe AS were assessed by HT and qualified to SAVR—26, TAVI—200 and OMT—17. No significant differences in age or perioperative risk assessed by EuroSCORE II between these three groups were observed. The authors reported that survival outcomes after TAVI and SAVR were similar with each other (93% vs. 84% for SAVR at 1 year and 85% vs. 84% for SAVR at 2 years) and similar to the age-matched general population with both being longer than for patients receiving only OMT (73% and 54% at 1– and 2–years, respectively, $p = 0.002$) [34]. A total number of 286 high-risk patients with AS discussed by HT and qualified for SAVR ($n = 53$), TAVR ($n = 210$) and OMT ($n = 23$) were prospectively evaluated with median (IQR) follow-up of 18 (11–26) months in the study of Tirado–Conte G, et al. The authors reported an increasing number of patients referred for HT discussion, with a 26% growth between study periods. Importantly, 20% of patients in the SAVR-cohort underwent a concomitant valve intervention. In-hospital mortality was 7.5% for SAVR, compared with 3.4% in the transfemoral TAVR group ($p = 0.447$). 1– and 2–year all-cause mortality did not significantly differ between SAVR and TAVR groups (14.0% vs. 17.2% for TAVR at 1 year and 17.2% vs. 25.9% at 2 years), while patients referred to OMT had the worst prognosis with only one-third survived 1– and 2–years [35].

In our retrospective study, we evaluated patients presented to our internal HT during a period of 4 years. Finally, 482 participants with severe AS and completely implemented HT decisions (OMT, TAVR and SAVR for 79, 318 and 85, respectively) were included and followed for adverse events with a period of about 2.5 years. SAVR and TAVR were found to be superior to OMT for primary (all-cause mortality, non-fatal disabling strokes and non-fatal rehospitalizations for AS) and all secondary endpoints ($p < 0.05$). Comparing interventional strategies only, TAVR was associated with a reduced risk of AKI, new onset of atrial fibrillation and major bleeding, while the superiority of SAVR for major vascular complications and need for permanent pacemaker implantation was observed ($p < 0.05$). The quality of life assessed at the end of follow-up was significantly better for patients who underwent TAVR or SAVR than in OMT-group ($p < 0.05$) [36]. Current evidence from observational studies summarizing the role of HT for treating patients with AS was presented in Table 2.

Table 2. Heart Team for aortic stenosis.

Study Type	Clinical Characteristics	Results	Ref. No.
prospective	163 high-risk patients with symptomatic AS: SAVR—35, TAVI—73, OMT/PTAV—55 Median (IQR) follow-up: 38 (12–42) months for SAVR, 25 (12–40) months for TAVI, 32 (18–41) months for OMT/PTAV	• 30-days overall mortality, CV death and stroke did not significantly differ between groups, whereas patients from SAVR group had statistically the highest 30-days incidence of life-threatening bleeding and new onset of AF. • TAVI and SAVR was significantly superior to OMT/PTAV for all-cause mortality and CV death and nonsignificantly superior to OMT/PTAV for repeat hospitalizations for CV cause at 1 year. • At 1 year: stroke/TIA and PPI were nonsignificantly more frequent in TAVI-group as compared with SAVR or OMT/PTAV, whereas in SAVR-group new onset of AF with the highest incidence was observed.	[31], Dubois C, et al.
retrospective	487 patients with severe AS: SAVR—392, TAVI—60, OMT—35 Median (IQR) follow-up: 3.5 (1.87–3.53) years	• Very poor prognosis for OMT-group with only 57.1 and 25.7% surviving to 1 and 3 years, respectively. • Survival after TAVI was lower but did not significantly differ from survival after isolated SAVR (88.3% vs. 92.6% at 1 year and 71.7% vs. 86.8% at 3 years, respectively), although TAVR-patients were older and with higher risk.	[32], Thyregod HGH, et al.
prospective	405 high-risk patients with AS: SAVR—98, TAVI—188, OMT/PTAV—116 Median follow-up: 12 months	• 30-days overall mortality and CV death was the most frequent in OMT/PTAV group. • TAVI and SAVR was significantly superior to OMT/PTAV for all-cause mortality and CV death at 1 year. • No differences in stroke/TIA and rehospitalization for CV cause between groups after 30 days and at 1 year were observed. • With the highest incidence: life-threatening bleeding at 30 days, PPI and new onset of AF after 30-days and at 1 year in SAVR-group; and major vascular complications in TAVI-group after 30 days and at 1 year were observed.	[33], Bakelants E, et al.
retrospective	243 patients with severe AS: SAVR—26, TAVI—200, OMT—17 Mean (SD) follow-up: 2.0 (1.4) years	• Survival outcomes after TAVI and SAVR were similar with each other and similar to the age-matched general population. • Both TAVI and SAVR-patients had significantly increased survival as compared with OMT-group at 1 and 2 years.	[34], Rea CW, et al.
prospective	286 patients with AS: SAVR—53, TAVR—210, OMT—23 Median (IQR) follow-up: 18 (11–26) months	• In-hospital: mortality, strokes and PPI did not significantly differ between SAVR and TAVR groups. • For interventional strategies, TAVR was associated with an increased in-hospital major vascular complications, whereas in SAVR-patients significantly higher incidence of in-hospital: bleeding complications, AKI and new onset of AF were observed. • 1- and 2-year all-cause mortality and CV mortality were significantly increased in OMT-group as compared with interventional strategies (SAVR or TAVR). • 1- and 2-year all-cause mortality and CV mortality did not significantly differ between SAVR and TAVR.	[35], Tirado-Conte G, et al.

Table 2. *Cont.*

Study Type	Clinical Characteristics	Results	Ref. No.
retrospective	482 patients with severe AS: SAVR—85, TAVR—318, OMT—79 Median follow-up: 866 days	• Interventional strategies (SAVR or TAVR) was found to be significantly superior to OMT for primary (all-cause mortality, non-fatal disabling strokes and non-fatal rehospitalizations for AS) and all secondary endpoints. • For interventional strategies, TAVR was associated with significantly reduced risk of AKI, new onset of AF and major bleeding, whereas in SAVR-patients significantly reduced incidence of major vascular complications and need for PPI were observed.	[36], Jonik S, et al.

AS—aortic stenosis, SAVR—surgical aortic valve replacement, TAVI—transcatheter aortic valve implantation, OMT—optimal medical therapy, PTAV—percutaneous transluminal aortic valvuloplasty, IQR—interquartile range, CV—cardiovascular, AF—atrial fibrillation, TIA—transient ischemic attack, PPI—permanent pacemaker implantation, SD—standard deviation, TAVR—transcatheter aortic valve replacement, AKI—acute kidney injury.

4. Heart Team for Mitral Regurgitation

The current evidence demonstrating prognosis of MR-patients treated surgically, percutaneously or with OMT is still scarce, and although multiple reports have published survival data, only a few have compared outcomes post interventional approaches or OMT. So far, two RCTs: EVEREST II—Endovascular Valve Edge-to-Edge Repair Study [37] and COAPT—Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy [38] has reported results of severe MR treatment. In the EVEREST II trial 279 patients with moderately severe or severe MR (grade 3+ or 4+) were randomly assigned to receive MitraClip (MC) or mitral valve (MV) surgery—repair or replacement in a 2:1 ratio. Although percutaneous repair was less effective at reducing MR than conventional surgery and patients from surgery cohort had significantly better outcomes at 12 months (primary endpoint—freedom from death, surgery for MV dysfunction, and from grade 3/4+ MR)—73% vs. 55% in MC-group, $p = 0.007$, both groups achieved similar improvements in clinical outcomes [37]. At 5 years, the rate of the composite endpoint of freedom from death, surgery for residual MR, or 3/4+ MR in the intention-to-treat population was 44.2% vs. 64.3% in the MC and surgical groups, respectively ($p = 0.01$), however, mortality rates did not favor surgical approach (20.8% vs. 26.8% for surgery, $p = 0.4$) [39]. In the COAPT study, 610 patients with HF and moderate—to–severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated OMT were randomized in a ratio 1:1 to receive MC with OMT or OMT only. At 24 months, MC with OMT approach as compared with OMT alone was associated with significantly improved outcomes: the annualized rate of all hospitalizations for HF (35.8% vs. 67.9%, respectively, $p < 0.001$) and overall mortality (29.1% vs. 46.1%, respectively, $p < 0.001$). The rate of freedom from device–related complications at 12 months was very high—96.6% ($p < 0.001$ for comparison with the performance goal) [38]. However, in these randomized studies, the involvement of HT for optimal decision-making for patients with symptomatic MR was not detailed. Although an approach of experienced HT was emphasized in current guidelines for VHD [6,7], the position of HT in the treatment of MR-patients is based only on experts' opinion and data from some observational studies. In the study by Heuts S, et al., 158 patients with MR were qualified after HT discussion to different treatment strategies—surgery (isolated or concomitant mitral valve replacement (MVR)—67 patients), transcatheter intervention (MC or mitral valve repair (MVP)—20 patients) or OMT (71 patients). 30-days mortality were 3 (4.4 %), 0 (0.0 %) and 3 (4.2 %) for surgery, MC/MVP and OMT, respectively. Using statistical analysis with a median follow-up of 450 days for the various treatment options, an improved survival for surgically treated patients was revealed [40].

In another research, Külling M, et al., presented observational single-center report of 400 patients managed for MR. Followed by HT decisions, 179 patients (44.8%) were treated using MC, 185 (46.2%) by MVP and 36 (9.0%) by MVR. Outcomes with mean follow-up (SD) time of 32.2 (17.6) months favored patients treated with MVP who had higher 4-year survival (HR 0.40 (95% CI 0.26 to 0.63), $p < 0.001$) and fewer combined endpoints (all-cause mortality, cardiovascular (CV) rehospitalization and MV reintervention) as compared with MVR and MC groups [41]. Very recently, Nia PS., et al., reported that dedicated mitral HT provide improved care for patients with MV disease. A total number of 1145 patients—641 managed by the dedicated mitral HT and 504 by the general HT were observed for adverse events. At 1 year, the mortality was 74 (14.7%) for the general HT as compared with only 57 (8.9%) for the dedicated mitral HT ($p = 0.002$). At 5 years, survival probability was measured as 0.74 for the dedicated HT as compared to 0.70 for the general HT ($p = 0.04$).

The limitation of this study could be its non-randomized character; however, this kind of approach seems to be not necessary as it is intuitively obvious that specialists provide better management than generalists [42]. We also reported our plot in this topic providing outcomes and quality of life of patients with severe MR consulted by our internal HT. With mean (SD) follow-up of 29 (15) months 157 individuals with severe MR and completely implemented HT decisions (OMT, MC or MVR for 53, 58 and 46 patients, respectively) were included. MVR and MC were significantly superior to OMT for primary endpoint (CV death) and all secondary endpoints—overall mortality, non-fatal MI, non-fatal strokes, non-fatal hospitalizations for HF exacerbation and any CV events ($p < 0.05$). However, for interventional strategy—no significant differences between MVR and MC approach were observed. At the end of follow-up, physical, mental and total qualities of life for all alive participants were significantly improved for MVR-patients, then for MC and the poorest in OMT-group [43]. Current evidence from observational studies summarizing the role of HT for treating patients with MR is presented in Table 3.

Table 3. Heart Team for mitral regurgitation.

Study Type	Clinical Characteristics	Results	Ref. No.
prospective	158 patients with MV pathology with or without concomitant cardiac disesase: Surgery—67 (MVR or MVP; isolated or concomitant), percutaneous—20 (MC or MVA), OMT—71 30-days mortality and MACCE An estimated (Kaplan-Meier) overall survival with median follow-up: 450 days	• 30-days mortality: surgery—4.4%, OMT—4.2%, percutaneous—0.0%. • 30-days MACCE (mortality, MI, reoperation for failure or surgical repair, stroke, renal failure, infection, sepsis): surgery—16.0%, percutaneous—5.0%. • 450-days overall survival: beneficial long-term outcomes for surgically treated patients and very poor prognosis for OMT-group (25.4 % overall mortality).	[40], Heuts S, et al.
retrospective	400 patients with MR: MVR—36, MVP—185, MC—179 Mean (SD) follow-up: 32.2 (17.6) months	• No significant difference in in-hospital mortality between MVR, MVP and MC. • MVP-patients with significantly higher 4-year survival and fewer combined endpoints (all-cause mortality, CV rehospitalization and MV reintervention) as compared with MVR and MC groups.	[41], Külling M, et al.
retrospective	1145 patients with MV disesase: 641—discussed by dedicated mitral HT (surgery—289, transcatheter—101, OMT—251); 504—discussed by general HT (surgery—285, MC—7, OMT—212) Median (IQR) follow-up: 41.1 (22.8–60.0) months	• No significant difference in 30-day mortality between patients discussed by dedicated mitral HT and general HT. • Rate of 1-year mortality significantly reduced and 5-year survival probability significantly increased for patients discussed by dedicated mitral HT as compared with general HT.	[42], Sardari Nia P, et al.

Table 3. *Cont.*

Study Type	Clinical Characteristics	Results	Ref. No.
retrospective	157 patients with severe MR: MVR—46, MC—58, OMT—53 Mean (SD) follow-up: 29 (15) months	• All-cause mortality, CV death, nonfatal MI, nonfatal stroke, nonfatal hospitalizations for HF and CV events/one patient significantly the most frequent in OMT-group. • No significant difference between MVR and MC for all-cause mortality, CV death, nonfatal MI, nonfatal stroke, nonfatal hospitalizations for HF and CV events/one patient. • No significant difference in in-hospital mortality between MVR and MC.	[43], Jonik S, et al.

HT—Heart Team, MV—mitral valve, MVR—mitral valve replacement, MVP—mitral valve repair, MC—MitraClip, MVA—mitral valve annuloplasty, OMT—optimal medical therapy, MACCE—major adverse cardiac or cerebrovascular event, MI—myocardial infarction, SD—standard deviation, IQR—interquartile range, CV—cardiovascular, HF—heart failure.

5. Limitations

As we noted in the introduction, currently the main limitation of the HT concept still remains the lack of well-founded, step by step-planned RCTs comparing the long-term outcomes of patients treated with and without the HT approach. To date, evidence of the advantages of implementing multidisciplinary decision-making has been derived mainly from expert opinion and observational studies without a comparator. Unfortunately, in most of the large studies we referenced in this manuscript, such as SYNTAX, SYNTAX II, PARTNER, PARTNER 1, NOTION, PARTNER 2, SURTAVI, EVEREST II or COAPT [10,14,24,27–30,37,38], the main theme is head-to-head comparison of various treatment options for myocardial revascularization, AS or MR, rather than an importance or specific role of HT in the management of patients with these diseases. Therefore, the performing of well-designed RCTs with hard clinical endpoints remains one of the most important perspectives for a future HT concept. Additionally, for patients with CAD and VHD, adherence to physician recommendations and regular drugs usage is very important factors of future prognosis and quality of life. Unfortunately, these parameters are very difficult to measure and often remain a matter of mutual trust between the doctor and the patient. Also, among the articles regarding HT that we have cited in this manuscript, this issue is overlooked and very rarely raised [10,14]. So, a proper qualitative assessment of adherence to medical recommendations is still an unexplored issue and adds to the limitations of our review.

6. Future Perspectives

In this review, we presented the most extensive summary of the established and emerging evidence for the role of HT for myocardial revascularization and VHD—predominantly AS and MR as randomized or at least observational studies concerning management of HT for other heart valve defects are still unavailable in the literature. We have described HT (1) as recommended by guidelines for selection of optimal treatment modalities for complex patients, (2) emphasized that RCTs are desirable for future evaluation of HT concept (although proper design of such studies will be difficult), (3) highlighted importance of HT for perioperative risk assessment, and (4) proved that HT through weighing-up of the risks and benefits of each strategy for individual patient may provide improved outcomes in real-life clinical practice. Nowadays, the COVID-19 pandemic has brought telemedicine to the forefront of medical care and we assume that in the future, the HT meetings will also be digital. The remote patient's management with HT aided by artificial intelligence may be the next step of the development of HT concept.

At this point, we need to underline that independently of future directions of HT, patient' preference should always be on first place and shared-decision making could ameliorate balancing between mortality benefit and other patients–related matters such as periprocedural complications, the length of in-hospital stay and quality of life.

However, knowledge alone is not sufficient for patients to feel comfortable stating their own preferences; rather, a clear invitation from specialists for shared-decision making must be expressed. The future concept of HT should be developed with optimization of PCI procedures (including functional assessment, intravascular ultrasound and improved techniques of chronic total occlusion management), minimally invasive valvular surgeries and using new drugs improving symptoms and survival. The improvement of HT collaboration (members' interactions, feedback algorithms and patient involvement in decision steps) and subsequent RCTs would increase the HT importance and its implication in real-life clinical conditions.

Despite all future HT evolutions, one should be constant: the patient should remain at the main centre of each HT.

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9. PODSUMOWANIE

Idea kardiogrupy (Heart Team) od wielu lat cieszy się niesłabnącą i stale wzrastającą popularnością w kardiologii. Mimo iż koncepcja wielodyscyplinarnego zespołu specjalistów podejmujących decyzje terapeutyczne u chorych z wielonaczyniową chorobą wieńcową lub zastawkową wadą serca jest generalnie przyjęta w środowisku medycznym jako narzędzie zapewniające chorym optymalne rokowanie i akceptowalną jakość życia, brak jest jednoznacznego konsensusu, jak specjaliści kardiogrupy powinni współdziałać, jakie są pożądane cele takiej współpracy, a co najważniejsze, długoterminowe wyniki kwalifikacji pacjentów i jakość życia chorych są nadal słabo zbadane.

W cyklu oryginalnych publikacji przedstawiono wyniki kwalifikacji kardiogrupy w referencyjnym, trzeciorzędowym ośrodku akademickim u chorych z wielonaczyniową chorobą wieńcową, zwężeniem zastawki aortalnej lub niedomykalnością zastawki mitralnej. Zgromadzone dane kliniczne, echokardiograficzne i angiograficzne obejmują dużą ilość zróżnicowanych kardiologicznie chorych, okres obserwacji jest wystarczająco długi, a jasno zdefiniowane i szczegółowo przedstawione punkty końcowe stanowią ogromną ilość wiedzy, którą można przełożyć się na sformułowanie daleko idących wniosków.

W artykule state of art przedstawiono najdokładniejsze podsumowanie publikacji, doniesień i badań klinicznych, podnoszących kwestię koncepcji kardiogrupy w rewaskularyzacji mięśnia sercowego i chorobach zastawkowych serca – głównie zwężeniu zastawki aortalnej i niedomykalności zastawki mitralnej (ponieważ randomizowane lub przynajmniej obserwacyjne badania dotyczące działalności HT w innych wadach zastawek serca są nadal niedostępne w piśmiennictwie). W artykule opisano kardiogrupę jako rekomendowane narzędzie służące do wyboru optymalnych metod leczenia u skomplikowanych kardiologicznie pacjentów, podkreślono, że randomizowane badania kliniczne (RCTs) są pożądane dla przyszłej ewaluacji koncepcji HT, podkreślono znaczenie kardiogrupy w ocenie ryzyka okołooperacyjnego, oraz wykazano, że specjaliści HT poprzez staranną i skoncentrowaną na pacjencie stratyfikację zysków i start płynących z wyboru konkretnej strategii mogą zapewnić optymalne wyniki leczenia.

W ostatnich dwóch latach pandemia COVID-19 wyprowadziła telemedycynę na czoło opieki medycznej i można zakładać, że w przyszłości spotkania kardiogrupy również będą mogły odbywać się mobilnie. Zdalne zarządzanie pacjentem wspomagane sztuczną inteligencją może być kolejnym krokiem w rozwoju koncepcji HT.

W tym miejscu należy podkreślić, że niezależnie od przyszłych kierunków rozwoju kardiogrupy, preferencje pacjenta powinny być zawsze na pierwszym miejscu, a wielodyscyplinarne podejmowanie decyzji może poprawić równowagę między korzyścią z wydłużonego życia, a innymi kwestiami dotyczącymi chorego, takimi jak: powikłania okołozabiegowe, długość pobytu w szpitalu i pozabiegowa jakość życia.

Jednakże wiedza i kompetencje specjalistów kardiogrupy nie są wystarczające, aby pacjenci czuli się komfortowo, wyrażając własne preferencje; powinno raczej istnieć domyślne zaproszenie specjalistów do wspólnego podejmowania decyzji

Przyszła koncepcja HT powinna być rozwijana w kontekście trzech głównych strategii leczenia: optymalizacji zabiegów przezskórnych (w tym oceny czynnościowej, ultrasonografii wewnątrznaczyniowej i ulepszonych technik leczenia przewlekłych okluzji), minimalnie inwazyjnych operacji zastawkowych i stosowania nowych leków poprawiających objawy i wydłużających życie. Również udoskonalenie wewnętrznej współpracy w gronie specjalistów kardiogrupy i przeprowadzenie RCTs zwiększyłoby znaczenie HT i zdefiniowało jego funkcjonowanie w codziennej praktyce klinicznej.

Pomimo wszystkich przyszłych kierunków rozwoju kardiogrupy, istota zespołu wielodyscyplinarnego powinna być stała: pacjent powinien pozostać w centrum każdej kardiogrupy.

9.1. Wnioski.

1. Koncepcja kardiogrupy jako wielodyscyplinarnego zespołu specjalistów podejmujących optymalne decyzje terapeutyczne u skomplikowanych kardiologicznie pacjentów ma ugruntowaną pozycję w świecie medycyny, jednakże opartą głównie na badaniach retrospektywnych i opinii ekspertów.

2. W cyklu publikacji oryginalnych dowiedziono, że wdrożenie strategii inwazyjnych starannie przedyskutowanych przez specjalistów kardiogrupy zapewnia lepsze wyniki leczenia, redukuje ryzyko powikłań okołozabiegowych i poprawia jakość życia pacjentów z ciężką chorobą wieńcową, zwężeniem zastawki aortalnej lub niedomykalnością zastawki mitralnej.

3. Ogromna heterogenność chorych, jak i stały rozwój nowych i udoskonalenie starszych metod diagnostycznych, interwencyjnych i zachowawczych implikuje dalsze badania w zakresie

koncepcji, funkcjonowania i roli kardiogrupy, w tym przeprowadzenie starannie zaplanowanych randomizowanych badań klinicznych.

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11. OŚWIADCZENIA WSPÓŁAUTORÓW

WARSZAWSKI UNIWERSYTET MEDYCZNY
MEDICAL UNIVERSITY OF WARSAW

I Katedra i Klinika Kardiologii
Kierownik Kliniki: prof. dr hab. med. Marcin Grabowski

Warszawa, 15.06.2022 r.

OŚWIADCZENIE O WSPÓŁAUTORSTWIE PUBLIKACJI

TYTUŁ ARTYKUŁU: Heart Team for Optimal Management of Patients with Severe Aortic Stenosis—Long-Term Outcomes and Quality of Life from Tertiary Cardiovascular Care Center.

AUTORZY: Szymon Jonik, Michał Marchel, Ewa Pędzich-Placha, Zenon Huczek, Janusz Kochman, Piotr Scisło, Paweł Czub, Radosław Wilimski, Piotr Hendzel, Grzegorz Opolski, Marcin Grabowski, Tomasz Mazurek

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   Podpis współautora (Ewa Pędzich-Placha):
   dr n. med. Ewa Pędzich
   KARDIOLOG
   2214542

4. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Zenon Huczek):
   Prof. dr hab. n. med.
   Zenon Huczek
   Specjalista chorób wewnętrznych
   KARDIOLOG
   1457205

5. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Janusz Kochman):

SP Centralny Szpital Kliniczny
ul. Banacha 1a, 02-097 Warszawa
tel. 0-22 59-92-958, faks: 0-22 59-91-957
e-mail: cardiology@wum.edu.pl

6. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

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12. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Tomasz Mazurek):

SP Centralny Szpital Kliniczny
ul. Banacha 1a, 02-097 Warszawa
tel. 0-22 59-92-958, faks: 0-22 59-91-957
e-mail: cardiology@wum.edu.pl

WARSZAWSKI UNIWERSYTET MEDYCZNY
MEDICAL UNIVERSITY OF WARSAW

I Katedra i Klinika Kardiologii
Kierownik Kliniki: prof. dr hab. med. Marcin Grabowski

Warszawa, 15.06.2022 r.

OŚWIADCZENIE O WSPÓŁAUTORSTWIE PUBLIKACJI

TYTUŁ ARTYKUŁU: Long-term outcomes and quality of life following implementation of dedicated mitral valve Heart Team decisions for patients with severe mitral valve regurgitation in tertiary cardiovascular care center.

AUTORZY: Szymon Jonik, Michał Marchel, Ewa Pędzich-Placha, Arkadiusz Pietrasik, Adam Rdzanek, Zenon Huczek, Janusz Kochman, Monika Budnik, Radosław Piątkowski, Piotr Scisło, Janusz Kochanowski, Paweł Czub, Radosław Wilimski, Piotr Hendzel, Marcin Grabowski, Krzysztof Jerzy Filipiak, Grzegorz Opolski, Tomasz Mazurek

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   Podpis współautora (Ewa Pędzich-Placha): dr n. med. Ewa Pędzich KARDIOLOG 2214542

4. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Arkadiusz Pietrasik): dr n. med. Arkadiusz Pietrasik specjalista chorób wewnętrznych kardiolog PWZ 1885652

5. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Adam Rdzanek):

SP Centralny Szpital Kliniczny
ul. Banacha 1a, 02-097 Warszawa
tel. 0-22 59-92-958, faks: 0-22 59-91-957
e-mail: cardiology@wum.edu.pl

WARSZAWSKI UNIWERSYTET MEDYCZNY
MEDICAL UNIVERSITY OF WARSAW

I Katedra i Klinika Kardiologii
Kierownik Kliniki: prof. dr hab. med. Marcin Grabowski

6. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Zenon Huczek): Prof. dr hab. n. med. Zenon Huczek Specjalista chorób wewnętrznych KARDIOLOG

7. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

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    Podpis współautora (Paweł Czub):

13. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Radosław Wilimski):

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ul. Banacha 1a, 02-097 Warszawa
tel. 0-22 59-92-958, faks: 0-22 59-91-957
e-mail: cardiology@wum.edu.pl

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Kierownik Kliniki: prof. dr hab. med. Marcin Grabowski

14. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Piotr Hendzel):

15. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Marcin Grabowski):

    5775048
    prof. dr hab. n. med.
    Marcin Grabowski
    specjalista chorób wewnętrznych
    kardiolog, hipertensjolog

16. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Krzysztof Jerzy Filipiak):

    Prof. dr hab. n. med.
    KRZYSZTOF J. FILIPIAK
    specjalista chorób wewnętrznych
    specjalista hipertensjolog
    farmakolog kliniczny
    KARDIOLOG
    9714796

17. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Grzegorz Opolski):

    Prof. dr hab. med. Grzegorz Opolski
    kardiolog

18. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Tomasz Mazurek):

    Tomasz Mazurek
    chorób wewnętrznych
    KARDIOLOG

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Kierownik Kliniki: prof. dr hab. med. Marcin Grabowski

Warszawa, 15.06.2022 r.

OŚWIADCZENIE O WSPÓŁAUTORSTWIE PUBLIKACJI

TYTUŁ ARTYKUŁU: Optimal Management of Patients with Severe Coronary Artery Disease following Multidisciplinary Heart Team Approach—Insights from Tertiary Cardiovascular Care Center.

AUTORZY: Szymon Jonik, Michał Marchel, Ewa Pędzich-Placha, Arkadiusz Pietrasik, Adam Rdzanek, Zenon Huczek, Janusz Kochman, Monika Budnik, Radosław Piątkowski, Piotr Scisło, Paweł Czub, Radosław Wilimski, Jakub Maksym, Marcin Grabowski, Grzegorz Opolski, Tomasz Mazurek

DANE BIBLIOMETRYCZNE ARTYKUŁU: International Journal of Environmental Research and Public Health 2022; 19(7): 3933. doi: 10.3390/ijerph19073933.

1. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 85 %.

   Podpis współautora (Szymon Jonik): Szymon Jonik

2. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Michał Marchel):

3. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Ewa Pędzich-Placha): dr n. med. Ewa Pędzich KARDIOLOG 2214642

4. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Arkadiusz Pietrasik): dr n. med. Arkadiusz Pietrasik specjalista chorób wewnętrznych kardiolog PWZ 1885652

5. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Adam Rdzanek):

SP Centralny Szpital Kliniczny
ul. Banacha 1a, 02-097 Warszawa
tel. 0-22 59-92-958, faks: 0-22 59-91-957
e-mail: cardiology@wum.edu.pl

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Kierownik Kliniki: prof. dr hab. med. Marcin Grabowski

6. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Zenon Huczek): Prof. dr hab. n. med. Zenon Huczek Specjalista chorób wewnętrznych KARDIOLOG 74572[illegible]5

7. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Janusz Kochman):

8. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Monika Budnik):

9. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Radosław Piątkowski):

10. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Piotr Scisło):

11. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Paweł Czub):

12. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Radosław Wilimski):

13. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

    Podpis współautora (Jakub Maksym):

SP Centralny Szpital Kliniczny
ul. Banacha 1a, 02-097 Warszawa
tel. 0-22 59-92-958, faks: 0-22 59-91-957
e-mail: cardiology@wum.edu.pl

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Kierownik Kliniki: prof. dr hab. med. Marcin Grabowski

14. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

Podpis współautora (Marcin Grabowski):

15. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

Podpis współautora (Grzegorz Opolski):

16. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

Podpis współautora (Tomasz Mazurek):

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I Katedra i Klinika Kardiologii
Kierownik Kliniki: prof. dr hab. med. Marcin Grabowski

Warszawa, 15.06.2022 r.

OŚWIADCZENIE O WSPÓŁAUTORSTWIE PUBLIKACJI

<u>TYTUŁ ARTYKUŁU:</u> An Individualized Approach of Multidisciplinary Heart Team for Myocardial Revascularization and Valvular Heart Disease—State of Art.

<u>AUTORZY:</u> Szymon Jonik, Michał Marchel, Zenon Huczek, Janusz Kochman, Radosław Wilimski, Mariusz Kuśmierczyk, Marcin Grabowski, Grzegorz Opolski, Tomasz Mazurek

<u>DANE BIBLIOMETRYCZNE ARTYKUŁU:</u> Journal of Personalized Medicine 2022; 12: 705. doi: 10.3390/jpm12050705.

1. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 92 %.

   Podpis współautora (Szymon Jonik):

2. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Michał Marchel):

3. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Zenon Huczek): Prof. dr hab. n. med. Zenon Huczek Specjalista chorób wewnętrznych KARDIOLOG

4. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Janusz Kochman):

5. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Radosław Wilimski):

SP Centralny Szpital Kliniczny
ul. Banacha 1a, 02-097 Warszawa
tel. 0-22 59-92-958, faks: 0-22 59-91-957
e-mail: cardiology@wum.edu.pl

6. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Mariusz Kuśmierczyk):

   KIEROWNIK
   Kliniki Kardiochirurgii
   Centralny Szpital Kliniczny UCK WUM

7. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Marcin Grabowski):

   5775048
   prof. dr hab. n. med.
   Marcin Grabowski
   specjalista chorób wewnętrznych
   hipertensjolog

8. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Grzegorz Opolski):

   3718998
   Prof. dr hab. med. Grzegorz Opolski
   specjalista chorób wewnętrznych
   kardiolog

9. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł: 1 %.

   Podpis współautora (Tomasz Mazurek):