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Rola przezskórnej balonowej walwuloplastyki zastawki aortalnej w leczeniu ciężkiej stenozy aortalnej

The role of balloon aortic valvuloplasty in the treatment of severe aortic stenosis

Praca doktorska

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Wprowadzenie

W krajach rozwiniętych stenoza aortalna (AS) jest najczęstszą nabytą wadą zastawkową serca. Częstość występowania AS u osób w wieku podeszłym (powyżej 75 roku życia) wynosi 12,4%, z czego częstość ciężkiej AS wynosi 3,4%.[1] Ciężka objawowa AS jest związana ze złym rokowaniem, gdyż większość pacjentów umiera w ciągu 2-3 lat od postawienia rozpoznania.[1,2] Preferowaną metodą leczenia ciężkiej objawowej AS jest chirurgiczna wymiana zastawki aortalnej (AVR), ale z powodu wysokiego ryzyka zabiegowego wielu pacjentów nie zostaje zakwalifikowanych do operacji kardiochirurgicznej.[3] Przezcewnikowa implantacja zastawki aortalnej (TAVI) i przezskórna balonowa walwulopastyka zastawki aortalnej (BAV) są mniej inwazyjnymi procedurami w porównaniu do operacji kardiochirurgicznej. TAVI zyskało szczególne zastosowanie jako akceptowalna, alternatywna metoda leczenia w grupie pacjentów wysokiego ryzyka operacyjnego. Jej zastosowanie w tej grupie pacjentów wiąże się z poprawą jakości życia i korzystnymi wynikami klinicznymi.[4,5] Wielkie nadzieje pokładano we wprowadzonej wiele lat przed TAVI metodzie BAV. Aczkolwiek, pierwsze publikacje wykazały, że jej wykonanie było związane z dużą liczbą powikłań oraz niezadowalającymi długoterminowymi wynikami klinicznymi i hemodynamicznymi.[6–8] Dzięki wprowadzeniu TAVI, postępowi technologicznemu i rosnącemu doświadczeniu operatorów aktualnie obserwuje się mniej powikłań po zbiegu BAV.[9,10] Zgodnie z wytycznymi Europejskiego Towarzystwa Kardiologicznego (ESC) dotyczącymi leczenia zastawkowych wad serca, BAV można rozważyć u chorych niestabilnych hemodynamicznie z wysokim ryzykiem operacyjnym jako zabieg pomostowy przed planowaną AVR lub TAVI, bądź u chorych z ciężką objawową AS, którzy wymagają pilnej rozległej operacji niekardiochirurgicznej (zalecenie klasy IIb, poziom wiarygodności C).[3] BAV można też rozważyć jako leczenie paliatywne

w indywidualnych przypadkach, kiedy ze względu na obecność ciężkich chorób współistniejących zabieg kardiochirurgiczny i TAVI są przeciwwskazane.[3] U pacjentów z towarzyszącą skurczową niewydolnością serca, znacznie obniżona frakcja wyrzutowa lewej komory (LVEF) stanowi istotne przeciwwskazanie do definitywnego leczenia. BAV może być szczególnie korzystny u tych pacjentów skutkując przejściową poprawą LVEF i ostatecznie zmianą kwalifikacji na TAVI/AVR.[11,12] W związku z tym, w erze TAVI, BAV zyskał nowe zastosowanie którym jest w szczególności pomostowanie pacjentów do leczenia definitywnego (TAVI lub AVR).[13–16]

Ponadto częste współistnienie choroby wieńcowej (CAD) z wadą zastawkową u starszych pacjentów może nastręczać dodatkowych trudności w leczeniu AS. Etiologia degeneracyjnej AS jest podobna do etiologii CAD i związana z procesami zapalnymi i zaburzeniami gospodarki wapniowej.[17] Dlatego prawie u połowy pacjentów w wieku ≥70 lat, nowo zdiagnozowana AS współistnieje z CAD.[18] Wytyczne ESC rekomendują wykonanie koronarografii przed planowaną operacją kardiochirurgiczną w przypadku: wywiadu CAD, podejrzenia niedokrwienia mięśnia sercowego, dysfunkcji skurczowej lewej komory, u mężczyzn >40 roku życia i u kobiet w okresie pomenopauzalnym lub u pacjentów z ≥1 czynnikiem ryzyka sercowo-naczyniowego (Klasa I, poziom wiarygodności C).[3] U pacjentów z wyjściowym wskazaniem do operacji zastawki aortalnej/mitralnej preferowaną metodą leczenia współistniejącej CAD jest zabieg pomostowania aortalno-wieńcowego (CABG) jeśli stopień zwężenia tętnicy wieńcowej wynosi ≥70% (Klasa I, poziom wiarygodności C).[3] Dlatego aktualnie metodą leczenia z wyboru u pacjentów z ciężką AS i współistniejącą CAD jest AVR z CABG. Wprowadzenie metody TAVI zapoczątkowało rozwój nowych złożonych modeli leczenia z dodatkowym wykorzystaniem przezskórnej angioplastyki wieńcowej (PCI) razem z BAV.[19–23] Dotychczasowe badania potwierdziły, że PCI jest wykonalne i bezpieczne u wybranej populacji pacjentów wysokiego ryzyka lub z przeciwwskazaniami do operacji

i z ciężką objawową AS.[21,23] U pacjentów zakwalifikowanych do TAVI najczęściej wybieraną metodą leczenia AS ze współistniejącą CAD jest leczenie etapowe z PCI, wykonywane przed TAVI.[19,23] Ponadto udowodniono, że jednoczasowe PCI i TAVI jest także bezpieczne i wykonalne.[19,22,23] Analogicznie pacjenci z istotną CAD oraz zakwalifikowani do BAV mogą być leczeni PCI w trakcie zabiegu BAV lub z etapowym PCI.[23] Jednakże istnieje mało danych dotyczących bezpieczeństwa BAV z jednoczasowym PCI.

TAVI poprawia przeżywalność i jakość życia u nieoperowalnych pacjentów w porównaniu z leczeniem zachowawczym ciężkiej AS. Z drugiej strony, jej zastosowanie wiąże się z wysokimi kosztami oraz możliwością wystąpienia specyficznych powikłań. Jednym z nich jest po-implantacyjny przeciek okołozastawkowy (PVL), który pozostaje istotnym powikłaniem pogarszającym kliniczne wyniki TAVI.[13,24] Obecność PVL stwierdza się u 70 % pacjentów u których wykonuje się TAVI, ale więcej niż łagodną PVL stwierdza się w przybliżeniu u 10-15% pacjentów.[4,25–27] Angiografia i echokardiografia są podstawowymi metodami do oceny stopnia PVL zaraz po implantacji protezy i mogą służyć do wytypowania pacjentów, którzy odnieśliby korzyść z optymalizacji wyniku zabiegu. Połączenie inwazyjnych pomiarów hemodynamicznych z oceną indeksu niedomykalności aortalnej (ARI) oraz technik obrazowania może być bardziej dokładne niż samo obrazowanie.[28,29] Balonowa post-dylatacja (PD) może zredukować PVL poprzez osiągnięcie lepszego rozprężenia protezy i optymalizacji uszczelnienia przestrzeni okołozastawkowej. Implantacja zastawki w zastawkę jest inną opcją leczenia istotnego PVL, szczególnie jeśli pozycja zaimplantowanej zastawki jest głębsza lub płytsza niż zaplanowana.[30–33] Jednakże dane na temat wpływu PD na długoterminowe wyniki leczenia po TAVI są skąpe.

Streszczenie pracy

Artykuł (1)

Acute and long-term outcomes of percutaneous balloon aortic valvuloplasty for the treatment of severe aortic stenosis.

Cel badania: Celem badania była ocena wyników okołozabiegowych i klinicznych BAV, oraz jej przydatności w podgrupach pacjentów z ciężką objawową AS i różnymi wskazaniami do BAV.

Metody i materiały: Do badania włączono 112 kolejnych pacjentów poddanych BAV od października 2012 r. do lipca 2015 r. Dane kliniczne i echokardiograficzne zostały zebrane w trakcie 1, 6, 12- miesięcznej obserwacji po BAV lub do czasu definitywnego leczenia – TAVI/AVR, przeszczepu serca lub śmierci. Wskazaniem do BAV z powodu ciężkiej AS była: (1) obecność objawów związanych z AS w klasie NYHA IV lub CCS IV; (2) wywiad omdleń; (3) pilna operacja niekardiochirurgiczna; (4) wstrząs kardiogenny; (5) obniżona LVEF <40% lub ekstremalnie niska zindeksowana powierzchni zastawki aortalnej (AVA) <0,4 cm^2 u pacjentów z klasą NYHA/CCS II-III. Wszyscy pacjenci mieli wykonane badanie echokardiograficzne przezklatkowe (TTE) przed zabiegiem BAV. Ciężką AS zdefiniowano jako AVA <1 cm^2 (zindeksowane AVA [cm^2/m^2 powierzchni ciała] <0,6 cm^2/m^2) i/lub średni gradient przez zastawkę aortalną ≥40 mmHg. Interdyscyplinarny Zespół Sercowy (Heart Team) składający się z doświadczonych kardiologów interwencyjnych, kardiochirurgów, nieinwazyjnych kardiologów oraz anestezjologów analizował przypadek każdego pacjenta

i decydował o dalszym leczeniu. Wyjątek stanowił pilny/ratunkowy BAV. Ryzyko operacyjne oceniano przy pomocy skal Society of Thoracic Surgeons Predicted Risk of Mortality (STS) i Logistic EuroScore II. Protokół badania został pozytywnie zatwierdzony przez Komisję Bioetyczną i od uczestników badania uzyskano pisemną zgodę.

Procedura: BAV był wykonywany pod kontrolą echokardiografii i fluoroskopii. Zastawkę aortalną osiągano z dostępu udowego używając koszulek naczyniowych 8-14 F oraz balonów TYSHAK NuCLEUS ™, TYSHAK®, TYSHAK II® PTV (NuMED Inc., Kanada) i VACS II (Osypka Medical Inc., Niemcy). Rozmiar balonów był dobierany na podstawie średnicy pierścienia aortalnego (18-28 mm) ocenianej w badaniu TTE lub echokardiogafii przezprzełykowej. W większości przypadków rozmiar balonu był o 1 mm mniejszy niż rozmiar pierścienia aortlanego. W prawej komorze umieszczano elektrodę enokawitrną uzyskując szybką stymulację komorową celem stabilizacji pozycji balonu i ochorny przed wystąpieniem bloków przedsionkowo-komorowych. Dostęp naczyniowy był zamykany przy użyciu systemu Angio-Seal 8F (St. Jude Medical, Inc., MN, USA) lub przy pomocy ucisku manualnego.

Obserwacja kliniczna: Po zabiegu BAV wizyta kontrolna z badaniem echokardiograficznym odbywała się w trakcie wizyty ambulatoryjnej lub telefonicznie, 1, 6 i 12 miesięcy po zabiegu lub do czasu wykonania TAVI/AVR/re-BAV lub stwierdzenia zgonu.

Wyniki: Łącznie analizie poddano 114 zabiegów BAV wykonanych u 112 pacjentów. Mediana wieku pacjentów wynosiła 84 lata (rozstęp międzykwartylowy, 79-87). Większość badanej populacji stanowiły kobiety. Łącznie 89,3% pacjentów było w klasie NYHA III lub IV. Obserwowano wysoką częstość nadciśnienia tętniczego, cukrzycy, choroby wieńcowej, wcześniejszych PCI, migotania przedsionków, przewlekłej choroby nerek. Mediana STS score wynosiła 8,0 (5,5-10,6)% i Euroscore II 8,1 (5,1-11,8)%.

Głównym wskazaniem do BAV był pomost do TAVI (n=58, 51,8%) i leczenie paliatywne (n=37, 33,0%). Pozostałymi wskazaniami do BAV był pomost przed pilnym zabiegiem chirurgii pozasercowej (n=9, 8,0%), pomost do AVR (n=6, 5,4%) i wstrząs kardiogenny (n=2, 1,8%). Podsumowując w trakcie obserwacji po zabiegu BAV 23 (20,5%) pacjentów miało wykonane TAVI oraz 11 (9,8%) pacjentów miało wykonany AVR. Dodatkowo u niektórych pacjentów, którzy byli zakwalifikowani do zabiegu BAV jak wyżej dochodziło do zmiany kwalifikacji w trakcie trwania obserwacji.

Jednoczasowa koronarografia z BAV została wykonana u 21 (18,7%) pacjentów, jednoczasowa PCI u 10 (8,9%) pacjentów. Całkowita ilość podanego kontrastu wynosiła 25 (0-50) ml dla BAV, 100 (50-150) ml dla BAV z koronarografią i 150 (30-200) ml dla BAV z PCI. Naczyniowego systemu zamknięcia użyto u 37 (33,0%) pacjentów. Średni czas hospitalizacji wyniósł 9,6 ± 6,3 dni.

W przezklatkowych badaniach echokardiograficznych wykonanych po zabiegu BAV oraz po 1, 6, 12 miesiącach obserwowano wzrost AVA (odpowiednio +0,23, +0,15, +0,05, +0,05 cm^2, $p<0,05$ dla wszystkich), spadek maksymalnego gradientu przez zastawkę aortalną (pAVG) (odpowiednio -28,6, -24,4, -8,7, -4,8 mmHg, $p<0,05$ dla wszystkich) w porównaniu z wartościami wyjściowymi. U pacjentów z obniżoną LVEF (n=34, 30,4%; LVEF <40%) po BAV obserwowano wzrost LVEF (mediana +16%) po 1 miesiącu ($p<0,05$) który utrzymywał się do 6 miesięcy po BAV. Pozytywna odpowiedź była obserwowana u 77% pacjentów.

Duże zdarzenia niepożądane wystąpiły u 21 pacjentów: a) zgon w trakcie procedury (n=3), b) tamponada (n=2), c) ciężka AR (n=1, w 12-miesięcznej obserwacji leczona skutecznie TAVI), d) ciężkie zaburzenia rytmu (n=5), e) implantacja kardiostymulatora (n=1), f) potrzeba przetoczenia koncentratu krwinek czerwonych: 1 jednostka u 3 pacjentów, 2 jednostki

u 5 pacjentów, 4 jednostki u 4 pacjentów, 5 jednostek u 1 pacjenta (n=13). Powikłania naczyniowe wystąpiły u 11 pacjentów (9,8%).

Śmiertelność okołoproceduralna, wewnątrzszpitalna oraz po 1, 6, 12 miesiącach wyniosła odpowiednio 2,7%; 8,9%; 8,9 %; 16,9%; 22,3%. W analizie jednoczynnikowej u kobiet częściej występowały powikłania naczyniowe niż u mężczyzn (14,3% vs. 2,4%, p=0,04). W analizie wieloczynnikowej regresji logistycznej wykazano, że jedynym niezależnym predyktorem 12-miesięcznej całkowitej śmiertelności jest STS score [ryzyko względne (HR) (95% CI) 1,130 (1,038 to 1,231); p=0,05].

Wnioski: BAV jest przydatną procedurą w przypadku pacjentów wysokiego ryzyka z ciężką AS, jednakże ograniczoną z powodu złych wyników długoterminowych. Ograniczenia dotyczą krótkotrwałej poprawy objawów klinicznych, parametrów hemodynamicznych i echokardiograficznych, aczkolwiek osiągnięte efekty mogą być wystarczające dla pomostowania pacjentów do TAVI/AVR. Nasze badanie dodatkowo dowodzi, że BAV u niektórych pacjentów skutkuje poprawą wyjściowo obniżonej LVEF (<40%). BAV u pacjentów nie kwalifikujących się wyjściowo do TAVI/AVR może być rozważany jako ostatnia opcja leczenia skutkująca zmniejszeniem objawów i/lub poprawą mobilności.

<u>Artykuł (2)</u>

In-hospital and long-term outcomes of percutaneous balloon aortic valvuloplasty with concomitant percutaneous coronary intervention in patients with severe aortic stenosis.

Cel badania: Celem badania była ocena komplikacji zabiegowych i wyników długoterminowych pacjentów z ciężką AS, u których wykonano zabieg BAV i PCI.

Metody i materiały: Do badania włączono 97 kolejnych pacjentów z objawową ciężką AS, u których wykonano 104 zabiegi BAV od grudnia 2013 r. do marca 2017 r. Wszyscy pacjenci byli zakwalifikowani do BAV lub do koronarografii i BAV przez interdyscyplinarny zespół specjalistów (Heart Team). PCI po koronarografii było wykonane u pacjentów prezentujących objawy niestabilnej dławicy, zawału mięśnia sercowego bez uniesienia odcinka ST i stabilnej dławicy piersiowej z angiograficznie istotnym zwężeniem tętnicy wieńcowej. Koronarografia nie była wykonywana ponownie jeśli obraz tętnic wieńcowych był znany (zabieg do 6 miesięcy wstecz, brak wywiadu wcześniejszych zabiegów PCI). Badanie zostało zatwierdzone przez lokalną Komisję Bioetyczną i wszyscy kwalifikujący się pacjenci podpisali pisemną zgodę. Ryzyko zabiegowe oceniono za pomocą skal logistic EuroSCORE II oraz STS score. Parametry wyjściowe, proceduralne jak i długoterminowe wyniki oceniono w trzech grupach – sam BAV, BAV z koronarografią i BAV z PCI.

Procedura: Ten sam dostęp udowy wykorzystywano przy jednoczasowej koronarografii/PCI, a następnie podczas zabiegu BAV aby osiągnąć pozycję zastawki aortalnej pod kontrolą echokardiografii i fluoroskopii. BAV był wykonywany gdy znana był już anatomia tętnic wieńcowych i istotne hemodynamicznie zmiany zostały zaopatrzone stentem/stentami.

Pacjentom z jednoczasową PCI podawano 600-mg klopidogrelu jako dawki nasycającej podczas procedury. Dostęp naczyniowym zamykano przy użyciu system zamknięcia naczyniowego Angio-Seal (St. Jude Medical, USA) lub przy pomocy ucisku manualnego.

Obserwacja kliniczna: Pacjenci byli obserwowani przez minimum 12 miesięcy lub do czasu ponownego BAV, leczenia definitywnego (TAVI/AVR) lub śmierci.

Wyniki: Spośród 97 pacjentów, 34 (35,0%) przebyło sam BAV, 45 (46,4%) przebyło BAV z koronarografią i 18 (18,6%) BAV z PCI. Nie stwierdzono różnic w charakterystyce wyjściowej i wskazaniach do BAV w badanych grupach (p>0,05). Prawie połowa pacjentów, która przebyła BAV z PCI miała wywiad wcześniejszych zabiegów PCI. U pacjentów z wykonaną jednoczasowo koronarografią lub PCI zauważono zastosowaną większą dawkę kontrastu, promieniowania i dłuższy czas fluoroskopii. Nie obserwowano zwiększonego ryzyka powikłań po BAV z koronarografią/PCI. Nie stwierdzono także różnic w długości pobytu w szpitalu (p=0,12). W okresie obserwacji 12-miesięcznej TAVI została wykonana u 13 (13,4%) pacjentów, a AVR została wykonana u 3 (3,1%) pacjentów. Pomimo braku różnic w śmiertelności szpitalnej (5,6% vs. 8,9%; p=0,76), u pacjentów którzy przebyli BAV z PCI obserwowano mniejszą długoterminową śmiertelność niż u pacjentów którzy przebyli BAV z koronarografią (28,5% vs. 51,0%; p=0,03). W wieloczynnikowym modelu regresji Cox'a skorygowanej o wiek, płeć i wskaźnik masy ciała, STS score został zidentyfikowany jako jedyny niezależny czynnik predykcyjny długoterminowej śmiertelności dla wszystkich pacjentów (HR 1,09, 95% CI 1,04-1,15; p=0,0006).

Wnioski: Pacjenci z BAV i jednoczasowym PCI mają lepsze przeżycie niż pacjenci z BAV i samą koronarografią. Jednoczasowe wykonanie PCI lub koronarografii z BAV nie zwiększa ryzyka dużych i naczyniowych powikłań BAV.

Artykuł (3)

Impact of post-dilatation on the reduction of paravalvular leak and mortality after transcatheter aortic valve implantation.

Cel badania: Celem badania była ocena efektów balonowej PD na redukcję okołozastawkowego przecieku i śmiertelność u pacjentów leczonych TAVI.

Metody i materiały: Do badania włączono 101 kolejnych pacjentów wysokiego ryzyka w wielu podeszłym z ciężką objawową AS, którzy przebyli TAVI pomiędzy listopadem 2008 r., a listopadem 2014 r. Wybór pacjentów był dokonywany przez wielodyscyplinarny Zespół Sercowy na podstawnie danych klinicznych i obrazowych. Protokół badania został zatwierdzony przez Komisję Etyczną.

Procedura: Zabiegi TAVI wykonywano z użyciem zastawek Edwards Sapien, Edwards Sapien XT, Edwards Sapien 3 (Edwards Lifesciences, Irvine, CA, USA) Medtronic Corevalve, EvolutR (Medtronic Inc., MN, USA), and JenaValve (JenaValve Technology, Niemcy). Użyto dostępu przezudowego, przezkoniuszkowego i bezpośredniego aortalnego. Po implantacji zastawki stopień PVL oceniano rutynowo przy użyciu aortografii. U wszystkich pacjentów wykonano pomiary hemodynamiczne i kalkulację ARI. U pacjentów z więcej niż łagodnym PVL ocenionym w aortografii i/lub ARI <25%, PVL oceniano echokardiograficznie, najlepiej echokardiografią przezprzełykową i w przypadku potwierdzenia jego obecności wykonywano PD. Aortografia, echokardiografia i ARI posłużyły do oceny ciężkości PVL przed i po PD. W przypadku zastawek montowanych na balonie, PD wykonywano przez zwiększenie o 1-2 cc ilości kontrastu w systemie balonu doprowadzającego. Dla zastawek samorozprężalnych użyto balonu (Osypka VACS II, Osypka AG, Niemcy) o średnicy w stosunku 1:1 do rozmiaru pierścienia aortalnego. Pacjenci zostali podzieleni na dwie grupy w zależności czy mieli

wykonane PD po TAVI. Następnie oceniono redukcję stopnia PVL, zmianę ARI i wyniki kliniczne.

Wyniki: Balonowa PD została wykonana u 23 (22,8%) pacjentów. Skuteczną redukcję PVL (brak lub łagodna PVL) zaobserwowano u 95,6% chorych. PD zwiększyło ARI z 23,4% (22,4–24,0) do 27,1% (26,1–28,3); p<0,001. Śmiertelność 30-dniowa wyniosła 14,1% w grupie bez PD vs. 0,0% w grupie z PD; p=0,07. Śmiertelność 1-roczna (21,8% vs. 4,3%; p=0,97) oraz częstość udarów (7,7% vs. 8,7%; p=0,99) nie różniła się między grupami.

Wnioski: Balonowa PD może być bezpieczną i skuteczną techniką redukcji umiarkowanego do ciężkiego PVL po TAVI. Zastosowanie PD wykazywało trend do redukcji śmiertelności 30-dniowej.

Introduction

Aortic stenosis (AS) is the most frequent acquired valve disease in developed countries. The prevalence of AS in the elderly (>75 years old) is 12.4% of whom 3.4% have severe AS.[1] Severe symptomatic AS is associated with a poor prognosis, as most patients die within 2–3 years of diagnosis.[1,2] Aortic valve replacement (AVR) is the preferred treatment of symptomatic AS but unavailable for many patients due to high procedural risk.[3] Transcatheter aortic valve implantation (TAVI) and balloon aortic valve valvuloplasty (BAV) are less invasive procedures as compared to surgery. TAVI is now given particular prominence in the group of high-risk patients as an acceptable alternative to AVR, with reported improvement in the quality of life and clinical outcomes.[4,5] There used to be high expectations for BAV, which was introduced many years before TAVI. However, first studies revealed that BAV was associated with high risk of complications as well as poor long-term clinical and haemodynamic outcomes.[6–8] Thanks to the introduction of TAVI, technological improvement and growing experience of the operators nowadays less complications after BAV are observed.[9,10] According to the European Society of Cardiology (ESC) guidelines for the management of valvular heart disease, BAV may be considered as a bridge to surgery or TAVI in haemodynamically unstable patients who are at high risk for surgery, or in patients with symptomatic severe AS who require urgent major non-cardiac surgery (recommendation class IIb, level of evidence C).[3] BAV may also be considered as a palliative procedure in selected cases when both surgery and TAVI are contraindicated because of severe comorbidities.[3] In patients with concomitant systolic heart failure, severely depressed left ventricular ejection fraction (LVEF) constitutes a significant risk factor against definitive treatment. BAV may be especially beneficial in those patients leading to temporary improvement of LVEF and requalification to TAVI/AVR.[11,12] Thus,

nowadays, in the era of TAVI, BAV has gained new indications particularly bridging patients to the final treatment (TAVI or AVR).[13–16]

Moreover frequent coexistence of coronary artery disease (CAD) and valvular disease in elderly patients, makes the treatment of AS more difficult. Etiology of degenerative AS reveals similarities to the etiology of CAD in inflammatory and calcific processes.[17] Therefore, in almost half of the patients aged 70 years or older, newly diagnosed AS coexists with CAD.[18] The ESC guidelines recommend to perform coronary angiography before valvular heart surgery in case of any of the following: history of CAD, suspected myocardial ischaemia, left ventricular systolic dysfunction, in men >40 years and postmenopausal women, or in patients with ≥1 cardiovascular risk factor (Class I, Level C).[3] In patients with a primary indication for aortic valve surgery, coronary artery bypass grafting (CABG) remains the preferred treatment of CAD if coronary artery diameter stenosis is ≥70% (Class I, Level C).[3] Therefore, until recently, the standard treatment option for patients with severe AS and concomitant CAD was AVR combined with CABG. After the introduction of TAVI, new complex models of treatment have been developed with the additional use of percutaneous coronary intervention (PCI) together with BAV.[19–23] The previous studies have confirmed that PCI is feasible and safe in a selected population of high-risk or inoperable patients with symptomatic severe AS.[21,23] For patients scheduled for TAVI, the most frequent approach to treat AS and coexisting CAD is staged PCI performed before TAVI.[19,23] Furthermore, concomitant PCI and TAVI have also been shown to be safe and feasible.[19,22,23] Similarly, patients with significant CAD scheduled for BAV can be treated with PCI at the time of BAV (as a single procedure) or with staged PCI.[23] However, data on the safety of BAV with concomitant PCI are scarce.

Although TAVI improves survival and quality of life in inoperable patients as compared to the medical treatment of severe AS, it is also associated with complications and high cost. The post-implantation paravalvular leak (PVL) remains an important TAVI-related

complication worsening outcomes.[13,24] PVL is present in up to 70% of all patients undergoing TAVI, and more than mild PVL has been reported in approximately 10–15% patients.[4,25–27] Angiography and echocardiography are the primary tools to quantify the degree of PVL after deployment of the prosthesis and selecting patients for optimization techniques. Combining haemodynamic measurements and imaging technique to assess PVL may be more accurate than imaging alone.[28,29] Balloon post-dilatation can reduce PVL by achieving a better expansion of the prosthesis and optimal sealing of the paravalvular space. Valve-in-valve implantation is another option to overcome significant PVL, especially if the implantation position is deeper or shallower than expected.[30–33] However, data on the impact of PD on long-term outcomes after TAVI are scarce.

Summary

Article (1)

Acute and long-term outcomes of percutaneous balloon aortic valvuloplasty for the treatment of severe aortic stenosis.

Aim: The aim of this study was to determine procedural and clinical outcomes of BAV, its usefulness in subgroups of patients with severe AS and different indications for BAV.

Methods: A total of 112 consecutive patients undergoing BAV due to severe symptomatic AS were enrolled between October 2012 and July 2015. Clinical and echocardiographic data were prospectively collected within 1, 6, and 12 months of follow-up or until definitive treatment-TAVI/AVR, heart transplantation or death. In accordance with our local experience, indications for BAV in severe AS included: (1) the presence of symptoms related to AS in New York Heart Association (NYHA) functional class IV and / or Canadian Cardiovascular Society (CCS) functional class IV; (2) history of syncope; 3) the need for urgent non-cardiac surgery; (4) cardiogenic shock; (5) impaired LVEF <40% or extremely low indexed valve area (AVA) <0.4 cm^2 in patients with NYHA/CCS functional classes II or III. All patients underwent transthoracic echocardiography (TTE) before the BAV procedure. Severe AS was defined as AVA <1 cm^2 (indexed AVA <0.6 cm^2/m^2 body surface area) and/or aortic valve (AV) mean gradient ≥40 mmHg in TTE.[3] An interdisciplinary Heart Team consisting of experienced interventional cardiologists, cardiac surgeons, non-invasive cardiologists and anesthesiologists, analyzed each patient's overall clinical situation to decide about further treatment, except emergent or salvage BAV. The preoperative risk was assessed using Society of Thoracic

Surgeons Predicted Risk of Mortality (STS) and the Logistic EuroScore II scores. The protocol of the study was approved by a local ethical committee and a written consent was obtained from participants.

Procedure: BAV was guided by TTE and fluoroscopy. AV was reached from a femoral retrograde approach using 8-14 F sheaths. Balloons TYSHAK NuCLEUS™, TYSHAK®, TYSHAK II® PTV (NuMED Inc.,Canada) and VACS II (Osypka Medical Inc., Germany) were used. The balloon size was chosen on the basis of annulus diameter (18-28 mm) assessed by transthoracic or transesophageal echocardiography. In most of the cases, the balloon size was 1 mm lower than aortic annulus. An endocavitary electrode was placed into the right ventricle to obtain rapid ventricular pacing, the balloon stabilization and to protect from atrioventricular block. The vascular puncture was closed with 8F Angio-Seal vascular closure device (St. Jude Medical, Inc., MN, USA) or with manual compression.

Clinical follow-up: After BAV, the clinical and echocardiographic follow-up visit was carried out at 1, 6, and 12 months or until TAVI/AVR, re-BAV or death.

Results: We analyzed a total of 114 BAVs performed in 112 patients. The median age was 84 years (interquartile range, 79-87) with a high prevalence of females. A total of 89.3% of patients were in NYHA class III or IV. The overall incidence of arterial hypertension, diabetes mellitus, coronary artery disease, previous PCI, atrial fibrillation, chronic renal insufficiency was high. Median STS score was 8.0 (5.5-10.6)% and Euroscore II score 8.1 (5.1-11.8)%.The leading indications for BAV were bridge for TAVI (n=58, 51.8%) and palliative treatment (n=37, 33.0%). Other indications included bridge for urgent non-cardiac surgery (n=9, 8.0%), bridge for AVR (n=6, 5.4%), and cardiogenic shock (n=2, 1.8%). To sum up, during follow-up, 23 (20.5%) of patients after BAV had TAVI and 11 (9.8%) AVR. In some cases patients who were at first qualified as described above, qualification has been changed during follow-up.

Concomitant coronary angiography was performed in 21 (18.7%) patients and resulted in PCI in 10 (8.9%) patients. Total contrast media volume was 25 (0-50) ml for BAV, 100 (50-150) ml for BAV with coronary angiography and 150 (30-200) ml for BAV with PCI. Vascular closure device was used in 37 (33%) patients. The average length of hospital stay was *9.6 ± 6.3* days. Echocardiograms performed after BAV and at 1, 6, 12 months showed an increase in AVA (+0.23, +0.15, +0.05, +0.05 cm^2, respectively, $p<0.05$ for all) and a decrease in pAVG -28.6, -24.4, -8.7, -4.8 mmHg, respectively, $p<0.05$ for all) as compared to baseline. In patients with LVEF< 40% (n=34, 30.4%) we observed a significant improvement in LVEF (median +16% in 77% patients) after 1 month ($p<0.05$) and this effect was significant up to 6 months after BAV. Major complications occurred in 21 patients and included: a) intraprocedural death (n=3), b) tamponade (n=2), c) severe AR (n=1, at 12 month, successfully treated with TAVI), d) severe cardiac arrhythmias (n=5), e) permanent pacemaker implantation (n=1), f) a need for red blood cells transfusion: 1 unit in 3 patients, 2 units in 5 patients, 4 units in 4 patients, 5 units in 1 patient (n=13). Vascular access site complications occurred in 11 patients (9.8%). Peri-procedural, in-hospital, 1-, 6-, and 12-month mortality were 2.7%; 8.9%; 8.9 %; 16.9%; 22.3%, respectively. In univariate analysis females had higher prevalence of *v*ascular complications than males (14.3% vs. 2.4%, p=0.04). In multivariate logistic regression analysis the only independent predictor of 12-month all-cause mortality was STS score [(hazard ratio (HR) of 1.130 per one STS point (95% CI 1.038-1.231; p=0.05)].

Conclusions: BAV is a useful procedure in high-risk patients with severe AS, nevertheless limited by poor long-term outcomes. The limitations concern intermittent improvement of symptoms, echocardiographic and hemodynamic parameters. However, achieved effects can be sufficient in bridging patients for TAVI/AVR. Our study provides additional evidence that BAV in patients with LVEF <40% may results in its recovery. BAV in patients not suitable for

TAVI/AVR, may be considered as the last option of treatment leading to symptomatic relief and/or improving mobility.

Article (2)

In-hospital and long-term outcomes of percutaneous balloon aortic valvuloplasty with concomitant percutaneous coronary intervention in patients with severe aortic stenosis.

Aim: The study aimed to evaluate procedural complications and long-term outcomes of patients with severe AS undergoing BAV and percutaneous coronary intervention (PCI).

Methods: We included 97 consecutive patients with severe symptomatic AS who underwent 104 BAVs between December 2013 and March 2017. All patients were qualified for BAV or BAV with coronary angiography by an interdisciplinary team of specialists (Heart Team). PCI after coronary angiography was performed in patients presenting with unstable angina, non ST-segment elevation myocardial infarction and stable angina with angiographically significant coronary artery stenoses. Coronary angiography was not performed if the patient had known coronary anatomy (procedure within the last 6 months, no previous PCI). The study was approved by a local ethical committee and all eligible patients signed the informed consent. The procedural risk was estimated by the EuroSCORE II and STS score. Baseline and procedural characteristics, as well as long-term outcomes were assessed in three groups - standalone BAV, BAV with coronary angiography (only), and BAV combined with PCI.

Procedure: The same femoral retrograde approach was used in case of concomitant coronary angiography/PCI and then during BAV to reach in aortic valve under echocardiographic and fluoroscopic guidance. BAV was proceeded once the coronary anatomy was known and hemodynamically significant lesions were treated with stent(s). Patients with concomitant PCI were given a 600-mg clopidogrel loading-dose during the procedure. A vascular access was

closed with Angio-Seal vascular closure device (St. Jude Medical, USA) or with manual compression.

Clinical follow-up: Patients were followed-up for at least 12 months or until the occurrence of repeated BAV, definitive treatment (TAVI/AVR) or death.

Results: Of the 97 patients, 34 (35.0%) underwent standalone BAV, 45 (46.4%) BAV with coronary angiography and 18 (18.6%) BAV with PCI. There were no differences in baseline characteristics and indications for BAV among the groups. Almost half of the patients who underwent BAV with PCI had a history of previous PCI. A higher contrast load, radiation dose and longer fluoroscopy time in patients with concomitant PCI or coronary angiography were noted. No higher risk of complications after BAV performed with concomitant coronary angiography/PCI was observed. No difference in the length of hospital stay was observed either). TAVI was performed in 13 patients (13.4%) and AVR in 3 (3.1%) patients during 12-month follow-up. In spite of no difference in in-hospital mortality (5.6% vs. 8.9%; p=0.76), patients with BAV and concomitant PCI had lower long-term mortality than patients with BAV and concomitant coronary angiography (28.5% vs. 51.0%; p=0.03). In multivariable Cox analysis adjusted for age, sex and body mass index, STS score was the only independent predictor of long-term mortality for all patients (HR 1.09, 95% CI 1.04-1.15; p=0.0006).

Conclusions: Patients with BAV and concomitant PCI have better survival than patients with BAV and concomitant coronary angiography. Concomitant PCI or coronary angiography performed with BAV does not increase the risk of major and vascular complications of BAV.

Article (3)

Impact of post-dilatation on the reduction of paravalvular leak and mortality after transcatheter aortic valve implantation.

Aim: The study aimed to evaluate the effects of balloon post-dilatation (PD) on the reduction of PVL and mortality in patients undergoing TAVI.

Methods: A total of 101 consecutive high-risk elderly patients with severe symptomatic AS undergoing TAVI were enrolled between November 2008 and November 2014. Patient selection for TAVI was performed by a multidisciplinary Heart Team supported by clinical and imaging resources. The study protocol was approved by the institutional Ethical Board.

Procedure: TAVI procedures were performed using Edwards Sapien, Edwards Sapien XT, Edwards Sapien 3 (Edwards Lifesciences, CA, USA) Medtronic Corevalve, EvolutR (Medtronic Inc., MN, USA), and JenaValve (JenaValve Technology, Germany). Access routes were transfemoral, transapical, and direct aortic. After valve deployment, the degree of PVL was routinely assessed by aortic root angiography. In all patients, haemodynamics were assessed and calculation of the aortic regurgitation index (ARI) was performed. In patients with more than mild angiographically detected PVL and/or an ARI <25%, PVL was evaluated by echocardiography, preferably transesophageal echocardiography, and if confirmed, a PD was performed. Angiography, echocardiography, and ARI were used to assess the severity of PVL before and after balloon PD. PD was performed by adding 1-2 cc of contrast dye to the delivery system of balloon expandable valves used during TAVI. For self-expandable prostheses, a 1:1 balloon to aortic native annulus was used for PD (Osypka VACS II, Osypka AG, Germany).

Patients were divided into two groups based whether or not PD after TAVI was performed. Reduction of PVL, change of ARI, and clinical outcomes were assessed.

Results: Balloon PD was performed in 23 (22.8%) patients. In 95.6%, PVL reduction was successful (no or mild PVL). PD increased the ARI from 23.4% (22.4–24.0) to 27.1% (26.1–28.3); p <0.001. Thirty-day mortality rate was 14.1% in the PD (–) group vs. 0.0% in the PD (+) group; p=0.07. One-year mortality (21.8% vs. 4.3%; p=0.97) and procedural stroke rate (7.7% vs. 8.7%; p=0.99) were not different between the groups.

Conclusions: Balloon PD may be a safe and effective technique to reduce moderate to severe PVL after TAVI. PD shows a trend toward lower mortality in a 30-day follow-up.

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VALVULAR AND STRUCTURAL HEART DISEASES

Original Studies

Acute and Long-Term Outcomes of Percutaneous Balloon Aortic Valvuloplasty for the Treatment of Severe Aortic Stenosis

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Objectives: This study aimed to evaluate the indications, short- and long-term outcomes of balloon aortic valvuloplasty (BAV) in patients with severe aortic stenosis (AS). Methods: A cohort of 112 patients with AS underwent 114 BAV procedures between October 2012 and July 2015 in two Polish interventional cardiology centers. Clinical and echocardiographic data were prospectively collected within 1, 6, and 12 months follow-up. Results: BAV was performed as a bridge to TAVI (51.8%), surgical aortic valve replacement (AVR, 5.4%), before urgent noncardiac surgery (8.0%), for symptom relief (33.0%) and cardiogenic shock (1.8%). Periprocedural, in-hospital, 1-, 6-, 12-month mortality were 2.7%; 8.9%; 8.9%; 16.9%; 22.3%, respectively. Serious periprocedural adverse events occurred in 18.8% of patients. After the procedure, mean aortic valve area (AVA) increased from 0.59 ± 0.18 to 0.82 ± 0.24 cm^2, mean peak aortic valve gradient (pAVG) decreased from 94.0 ± 27.6 to 65.4 ± 20.0 mm Hg, mean aortic gradient decreased from 58.0 ± 17.8 to 40.5 ± 14.6 mm Hg, $P < 0.05$ for all. Left ventricular ejection fraction (LVEF) increased from median (interquartile range) of 53.5 (30 – 64) to 60 (45 – 65)% after 1 month ($P < 0.05$). In patients with impaired left ventricle function (LVEF <40%), LVEF significantly improved (median increase of 16%) after 1 and 6 months ($P < 0.05$). At 12 months patients had higher AVA, pAVG, and LVEF as compared to baseline ($P < 0.05$). Conclusions: BAV is a useful procedure in high-risk AS patients, where achieved effects can be sufficient in bridging patients for TAVI/AVR.

Key words: balloon aortic valvuloplasty; aortic stenosis; transcatheter aortic valve implantation; surgical aortic valve replacement

INTRODUCTION

Aortic stenosis (AS) is the most frequent acquired valve disease in developed countries. The prevalence of all AS in the elderly (>75 years old) is 12.4% and the prevalence of severe AS is 3.4% [1]. Aortic valve replacement (AVR) is a preferred but unavailable treatment for many patients due to a high procedural risk. Transcatheter aortic valve implantation (TAVI) and balloon aortic valve valvuloplasty (BAV) are less invasive procedures as compared to surgery. TAVI is now given particular prominence in the group of high-risk patients as acceptable alternative to AVR [2] with improved quality of life [3] and clinical outcomes [4].

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Conflict of interest: Nothing to report.

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The old studies revealed that BAV had high risk of complications as well as poor haemodynamic and long-term clinical outcomes [5–7]. According to current European Society of Cardiology guidelines for the management of valvular heart disease, BAV may be considered as a bridge to surgery or TAVI in haemodynamically unstable patients who are at high risk for surgery, or in patients with symptomatic severe AS who require urgent major noncardiac surgery (recommendation class IIb, level of evidence C) [8]. BAV may also be considered as a palliative option for selected patients with AS and contraindications for surgery and TAVI due to severe comorbidities [6]. In addition, patients with a depressed left ventricular ejection fraction (LVEF) are frequently not scheduled for definitive treatment by AVR or TAVI due to a high risk of complications. In those patients BAV may allow for a temporary increase in LVEF and possible schedule for TAVI/AVR. Nowadays, in the era of TAVI, based on growing experience of the operators and considerable improvement of the equipment BAV seems to be a safe procedure. Thus, indications for BAV might be expanded particularly for bridging high-risk patients to the final treatment with TAVI or AVR. The aim of this study was to determine procedural and clinical outcomes of BAV, its usefulness in subgroups of patients with severe AS and different indications for BAV.

METHODS

Data Collection and Follow-Up

This study is an observational, prospective registry of patients undergoing BAV, conducted in two high volume centers experienced in diagnostics and treatment of AS including AVR and TAVI. One hundred twelve consecutive patients undergoing BAV due to severe symptomatic AS were enrolled between October 2012 and July 2015. In accordance with our local experience, indications for BAV in severe AS included: (1) presence of symptoms related to AS in New York Heart Association (NYHA) functional class IV and/or Canadian Cardiovascular Society (CCS) functional class IV; (2) history of syncope; 3) the need for urgent noncardiac surgery; (4) cardiogenic shock; (5) impaired LVEF <40% or extremely low indexed valve area (AVA) <0.4 cm2 in patients with NYHA/CCS functional class II-III. Data were collected using medical records containing demographic characteristics, information about cardiovascular risk factors, comorbidities, previous treatment, outpatient visits and telephone interviews. After discharge patients were followed for 1, 6, 12 months or up to definitive treatment - TAVI/AVR, heart transplantation or death. All patients underwent a transthoracic echocardiography (TTE) before the BAV procedure. Severe AS was defined as AVA <1 cm^2 (indexed valve area <0.6 cm^2/m^2 body surface area) and/or aortic valve (AV) mean gradient ≥ 40 mm Hg in TTE measured before or during hospitalization for BAV [8]. An interdisciplinary Heart Team consisting of experienced interventional cardiologists, cardiac surgeons, noninvasive cardiologists and anesthesiologists, analyzed each patient's overall clinical situation to decide about further treatment except emergent/salvage BAV. The preoperative risk was assessed using Society of Thoracic Surgeons Predicted Risk of Mortality (STS) and the Logistic EuroScore II predictive models. We used Bleeding Academic Research Consortium (BARC) classification for bleeding complications [9]. The protocol of the registry was approved by local ethical committee and written consent was obtained from all participants.

Procedure

BAV was guided by echocardiography and fluoroscopy. Aortic valvuloplasty was performed via transfemoral retrograde approach using $8-14$ F sheaths. Unfractionated heparin was given to achieve an activated clotting time of 250 to 300 sec. Balloons TYSHAK NuCLEUS ™, TYSHAK®, TYSHAK II® PTV from NuMED Inc. (Canada) and VACS II from Osypka Medical Inc. (Germany) were used during the study. The ballons' size was chosen on the basis of annulus diameter (18-28 mm) assessed in TTE or transesophageal echocardiography. In most of the cases, it was 1 mm lower than aortic annulus. In patients with bulk aortic leaflet calcification, we selected a balloon which was 2 mm smaller than the measured aortic annulus. An endocavitary electrode was placed in the right ventricle to obtain rapid ventricular pacing for balloon position stabilization and as a protection in case of atrioventricular blocks. The type of the balloon used and number of balloon inflations were at the discretion of the operator. Vascular punctures were closed with 8F Angio-Seal vascular closure device (St. Jude Medical, Inc., MN) or with manual compression. In patients who had not undergone angiography, BAV was performed during the same procedure following diagnostic angiography and percutaneous coronary intervention (PCI), if necessary. Adverse events during the procedure were defined as death, stroke, myocardial infarction, complete atrioventricular block, tamponade, pulmonary oedema, hemorrhage requiring transfusion, conversion to open heart surgery, acute severe aortic regurgitation (AR), severe ventricular arrhythmias. Post-procedural major complications were defined as death (both all-cause and cardiovascular), myocardial

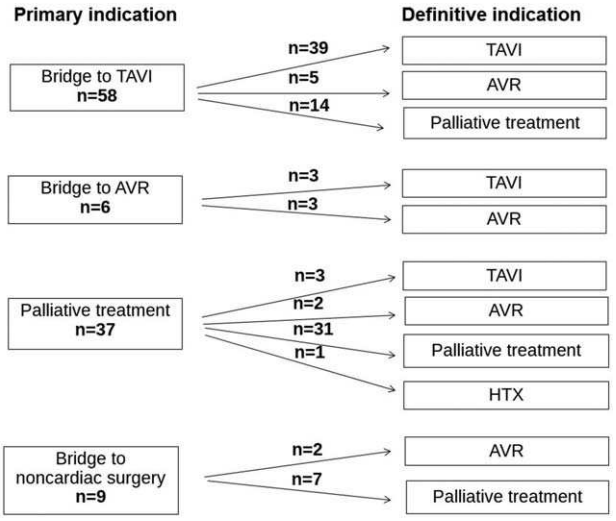

Fig. 1. Primary and definitive indications for balloon aortic valvuloplasty during follow up. TAVI denotes transcatheter aortic valve implantation; AVR, aortic valve replacement; HTX, heart transplantation.

infarction, stroke, episodes of decompensation requiring hospitalization, permanent pacemaker requirement, life-threating, or major bleeding [9].

Echocardiographic Data

Pre, post-BAV and 1-, 6-, 12-month follow-up echocardiograms were performed by the same experienced echocardiographers using GE Vivid E9 Ultrasound GE Vingmed Ultrasound AS, Horten, Norway. Measurements of AVAs (continuity equation), peak (pAVG) and mean AV gradients (mAVG), degree of ARs and LVEFs were based on M-mode, Doppler and 2-dimensional conventional echocardiography [8].

Statistical Methods

Continuous variables were expressed as mean (standard deviation) or median (interquartile range or minimum/maximum value). Normality was checked by Kolmogorov–Smirnov test. Continuous variables were compared by *t*-test for dependent samples when normally distributed or by Wilcoxon signed-rank test when not normally distributed. Categorical variables were expressed as number (percentage) and compared by Pearson's χ^2 test and Fisher's exact test. To test the association between two variables, the Pearson rank correlation coefficient for normally distributed variables or Spearman's rank correlation coefficient for not normally distributed variables were calculated. To identify independent predictors of vascular complications (VC) clinical, and laboratory variables that showed the association with VC in univariate model ($p < 0.05$) and did not show substantial correlations ($r > 0.5$) with another independent variable were then included in the multiple linear regression analysis. In addition, multivariable logistic regression analysis was performed to find significant predictors of 12-month mortality. Forward selection in multivariable logistic regression with a probability value for covariates to enter the model was set at the 0.05 level. All baseline clinical and echocardiographic, as well as procedural characteristics were tested. Results were presented as odds ratios (OR) with 95% confidence intervals (CI). All tests were 2-tailed, and a P value <0.05 was considered statistically significant. Data analysis was performed using STATISTICA 10.0 package (StatSoft Inc., Tulsa, OK).

RESULTS

Since October 2012 until July 2015 a total of 114 BAVs in 112 patients were performed. Repeat BAV was performed in 2 patients. The leading indication for BAV was a bridge for TAVI ($n = 58$, 51.8%). Other most common indications were bridges for AVR ($n = 6$, 5.4%) and palliative treatment ($n = 37$, 33.0%). Two patients (1.8%) underwent BAV because of cardiogenic shock and in 9 (8%) patients BAV was performed before urgent noncardiac surgery. To sum up, during follow-up, 23 (20.5%) of patients after BAV underwent TAVI and 11 (9.8%) patients underwent AVR. In some patients who were at first qualified as described above, qualification has changed during follow-up (Fig. 1).

Baseline Characteristics

The median age of enrolled population was 84 years (interquartile range, 79 – 87) with high prevalence of females. A total of 89.3% of patients were in NYHA class III or IV. Overall prevalence of arterial hypertension, diabetes mellitus, coronary artery disease, previous PCI, atrial fibrillation, chronic renal insufficiency was high (Table I). Median of STS score was 8.0 (5.5 – 10.6)% and Euroscore II 8.1 (5.1 – 11.8)%.

Procedural Data

Concomitant coronary angiography with BAV was performed in 21 (18.7%) patients and entailed concomitant PCI in 10 (8.9%) patients. Median, minimum/maximum values of balloon size were 22 (18 – 28) mm, number of inflations 2 (1 – 5), sheath size for femoral approach 9 (8 – 14) F, heparin dose 5,000 (1,000 – 8,000) IU, procedure length 30 (15 – 100) min, fluoroscopy time 10 (2 – 33 min), and radiation dose of 0.23 (0.01 – 3.7) Gy. Total contrast media volume was 25 (0 – 50) ml for BAV, 100 (50 – 150) ml

for BAV with coronary angiography and 150 (30 – 200) ml for BAV with PCI. Vascular closure device was used in 37 (33%) patients. The average length of hospital stay was 9.6 ± 6.3 days.

TABLE I. Baseline Characteristics

Variable	Value ($n = 112$)
Age, median (IQR) (years)	84 (79 – 87)
Women, *n* (%)	70 (62.5)
BMI, mean ± SD (kg/m^2)	18.5 ±3.5
Arterial hypertension, *n* (%)	98 (87.5)
Diabetes mellitus, *n* (%)	50 (44.6)
Coronary artery disease, *n* (%)	94 (83.9)
Previous myocardial infarction, *n* (%)	51 (45.5)
Previous PCI, *n* (%)	40 (35.7)
Previous CABG, *n* (%)	7 (6.3)
Cerebrovascular events, *n* (%)	19 (17.0)
Atrial fibrillation, *n* (%)	51 (45.5)
Peripheral vascular disease, *n* (%)	22 (19.6)
Previous peripheral artery intervention, *n* (%)	5 (4.5)
Chronic kidney disease, *n* (%)	65 (58.0)
COPD/asthma, *n* (%)	17 (15.2)
Neoplasm, *n* (%)	14 (12.5)
Previous radiotherapy, *n* (%)	2 (1.8)
Porcelain aorta, *n* (%)	3 (2.7)
Presenting symptom	
NYHA class I, *n* (%)	1 (0.9)
NYHA class II, *n* (%)	11 (9.8)
NYHA class III, *n* (%)	49 (43.8)
NYHA class IV, *n* (%)	51 (45.5)
CCS class IV, *n* (%)	6 (5.4)
Previous heart failure decompensation, *n* (%)	41 (36.6)
Syncope, *n* (%)	13 (11.6)
Shock, *n* (%)	2 (1.8)

Data are numbers (percentages) or medians (IQR). BMI denotes body mass index; PCI, percutaneous coronary interventions; CABG, coronary artery bypass graft surgery, COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association functional class; CCS, Canadian Cardiovascular Society functional class.

Echocardiographic Data and Clinical Symptoms

All echocardiographic baseline and follow-up parameters are listed in Table II. Echocardiograms performed after BAV and at 1, 6, 12 months showed that AVA was higher (+0.23, +0.15, +0.05, +0.05 cm^2, respectively, $P < 0.05$ for all) and pAVG was lower −28.6, −24.4, −8.7, −4.8 mm Hg, respectively, $P < 0.05$ for all) as compared to baseline. We observed a decrease in AVA at 6 months and 12 months (both −0.19 cm^2, $P < 0.05$) and an increase in pAVG at 6 months (+19.9 mm Hg, $P < 0.05$) and 12 months (+23.8 mm Hg, $P < 0.05$) as compared to values after BAV. Interestingly, mAVG was lower after BAV (−17.5 mm Hg, $P < 0.05$) and in 1 month follow up (−14.6 mm Hg, $P < 0.05$) compared with baseline. In 34 (30.4%) patients with impaired left ventricular function (LVEF <40%) a significant improvement of LVEF (median +16%) after 1 month ($P < 0.05$) was observed. This effect was stable up to 6 months after BAV (Fig. 2). A response to BAV (improvement in LVEF) was observed in 77% patients, without any progress of LVEF impairment due to BAV. This fact led to change of qualification to definitive therapy in three patients: one to AVR and two to TAVI. We did not recorded LVEF improvement immediately after BAV. An increase in LVEF was not correlated with change of AVA ($r = -0.50$, $P > 0.05$), peak AVG ($r = 0.01$, $P > 0.05$), or mean AVG ($r = -0.29$, $P > 0.05$). Right ventricular systolic pressure decreased directly after BAV (−9.1 mm Hg, $P < 0.05$). Table II presents change of AR after BAV and in 1, 6, 12 months of follow-up. There was one severe AR after 12 months and patient was successfully treated with TAVI. A significant improvement in symptoms was confirmed (Fig. 3).

TABLE II. Echocardiographic Data Before and After BAV and at 1-, 6-, 12-Month Follow-Up

Variable	Baseline ($n = 112$)	After BAV ($n = 77$)	1-month follow-up ($n = 44$)	6-month follow-up ($n = 42$)	12-month follow-up ($n = 23$)
AVA (cm^2)	0.59 ± 0.18	0.82 ± 0.24[a]	0.74 ± 0.21[a]	0.63 ± 0.17[a]‡	0.63 ± 0.17[a]
pAVG (mmHg)	94.0 ± 27.6	65.4 ± 20.0[a]	69.6 ± 23.7[a]	85.3 ± 25.2[a]‡	89.2 ± 32.9[a]‡
mAVG (mmHg)	58.0 ± 17.8	40.5 ± 14.6[a]	43.4 ± 17.4[a]‡	53.6 ±18.1‡	51.0 ± 7.7‡
LVEF (%)	53.5 (30 – 64)	57 (39 – 65)	60 (45 – 65)[a]	60 (50 – 65)[a]	60 (50 – 65)[a]‡
LVEF <40%(%)	25 (23 – 30)	25 (23 – 40)	41 (30.5 – 50)[a]	41.5 (30 – 50)[a]	45 (35 – 50)
RVSP (mmHg)	53.0 ±12.1	43.9 ±13.5[a]	57.3 ±14.9	60.6 ±17.2	49.0 ±20.2
Aortic regurgitation					
none/trivial, n (%)	33 (38.3)	14 (22.6)	11 (26.2)	9 (22.0)	7 (30.4)
mild, n (%)	41 (47.7)	31 (50.0)	23 (54.8)	25 (61.0)	11 (47.9)
moderate, n (%)	12 (14.0)	16 (25.8)	8 (19.0)	7 (17.0)	4 (17.4)
severe, n (%)	0 (0.0)	1 (1.6)	0 (0.0)	0 (0.0)	1 (4.3)

[a]P <0.05 compared with baseline, ‡P < 0.05 compared after BAV; LVEF denotes left ventricular ejection fraction; AVA, aortic valve area; pAVG, peak aortic valve gradient, mAVG, mean aortic valve gradient, RVSP, right ventricular systolic pressure.
Data are means ±SD or medians (IQR) unless otherwise stated.

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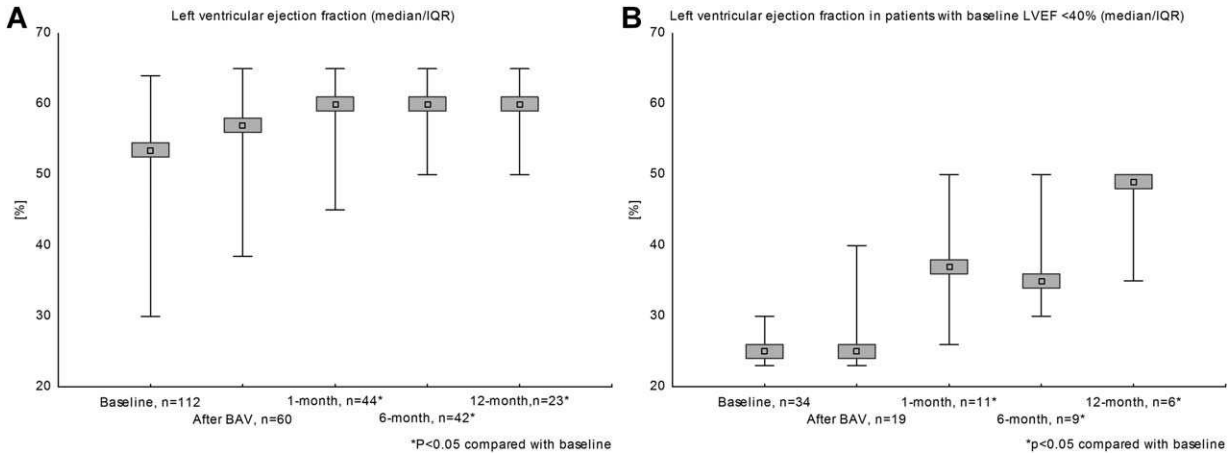

Fig. 2. Left ventricular ejection fraction at baseline and follow-up for all patients (A) and patients with baseline left ventricular ejection fraction <40% (B) Data are median/IQR.

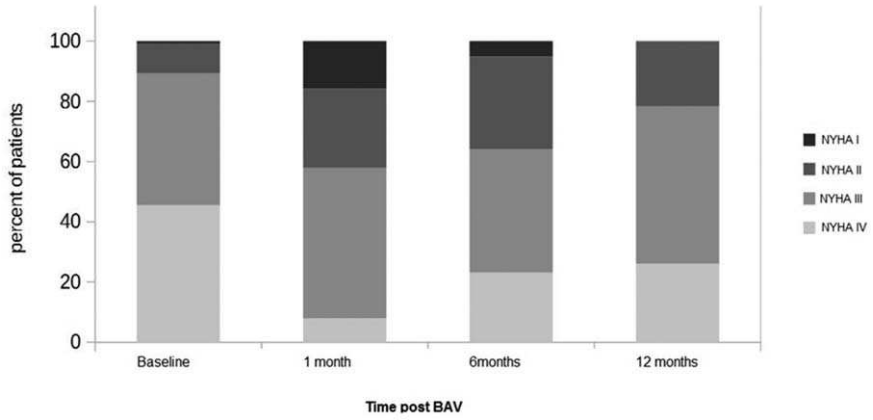

Fig. 3. New York Heart Association (NYHA) functional class at baseline and at follow-up. BAV denotes balloon aortic valvuloplasty.

BAV Complications and Mortality

Major complications occurred in 21 patients: (a) intraprocedural death ($n=3$), (b) tamponade ($n=2$), (c) severe AR ($n=1$), (d) severe cardiac arrhythmias ($n=5$), (e) permanent pacemaker implantation ($n=1$), (f) need for red blood cells transfusion: 1 unit in 3 patients, 2 units in 5 patients, 4 units in 4 patients, 5 units in 1 patient ($n=13$). From total amount of four tamponades, two resulted in intraprocedural death, one with conversion to AVR and one was successfully treated with pericardiocentesis. Complete atrioventricular block despite stimulation was the cause of third intraprocedural death. Vascular access site complications occurred in 11 patients (9.8%) including pseudoaneurysm ($n=6$) and hematoma ($n=5$), in one case leading to unplanned surgical repair of femoral artery and one retroperitoneal bleeding with open surgery. Patients with VC had lower hemoglobin (9.0 vs. 10.4 g/dL) and hematocrit levels (27.8 vs 31.2%) after BAV than the patients without VC (all $P<0.05$). In univariate analysis females had higher prevalence of VC than males (14.3% compared with 2.4%, $P=0.04$). This remained insignificant after adjusting for age and body mass index.

We did not record any case of stroke after BAV. However, we cannot exclude possible silent microembolism as head computed tomography and head magnetic resonance imaging scan were not performed routinely after BAV.

BAV primary indications and definitive indication during follow-up are shown in Fig. 1. Number of deaths (mortality rate) at 1, 6, 12 months was 10 (8.9%), 19 (16.9%), 25 (22.3%), respectively (Table III). Death were classified as cardiovascular in 14 (73.7%) cases (recurrent heart failure, sudden death, major stroke, pulmonary embolism) and noncardiovascular in 5 (26.3%) cases (cancer, major gastrointestinal bleeding). Patients who were treated with BAV due to

TABLE III. Mortality Data: Cumulative Follow-Up Mortality Rate

Variable	Value[c]
Procedural mortality rate[a]	3 (2.7%)
In-hospital mortality rate[b]	10 (8.9%)
30-day mortality rate	10 (8.9%)
6-month mortality rate	19 (16.9%)
12-month mortality rate	25 (22.3%)

[a]Due to procedural complications.
[b]All-cause in-hospital death, including procedural.
[c]$n = 112$ patients, $n = 114$ procedures.
Data are numbers (percentages).

cardiogenic shock had the worst prognosis with 100% mortality in this group [10]. Mortality rate was also high among palliative patients $n = 9$ (41%). Of 37 palliative patients one patient was qualified for heart transplantation, 3 has changed qualification for TAVI and 2 subsequently underwent TAVI; 2 were qualified for AVR and subsequently underwent AVR. In the subgroup of patients eventually bridged for TAVI (Fig. 1): 20 successfully underwent TAVI, 15 died before intended procedure and 14 were excluded due to progressive dementia, mitral stenosis, malignancy or severe impairment of mobility. Five patients who were intended to undergo TAVI were switched to AVR because of concomitant severe tricuspid regurgitation, large aortic annulus and improvement of LVEF after BAV. Six patients were bridged for AVR. Of them 2 patients underwent AVR, 1 patient died, and 3 patients were requalified for TAVI (2 of them underwent that procedure). All patients bridged to noncardiac surgery successfully underwent their intended procedures, in 2 patients AVR was performed after noncardiac procedure. The rest of assessed patients remained in palliative treatment. Of them 2 patients died. Four patients were lost to clinical follow-up. To summarize 71.1% of patients after BAV as a bridge to TAVI/AVR maintained qualification and in 60% with maintained qualification intended procedures were performed. In the group with palliative BAV 16.2% was successfully converted to TAVI/AVR/HTX and 66.6% underwent these intended procedures. In the group of patients who underwent BAV as a bridge to noncardiac surgery 22.2% were converted and had AVR while the rest remained palliative.

Adverse events during observation occurred in 38 (33.9%): life-threatening or major bleeding ($n = 2$), implantation of permanent pacemaker ($n = 3$), recurrent hospitalizations for decompensated heart failure ($n = 20$), reBAV ($n = 2$), diagnosis of cancer ($n = 2$), PCI ($n = 4$), resuscitated sudden cardiac arrest ($n = 2$), diagnosis of thrombus in the heart ($n = 2$). In multivariable logistic regression analysis the only independent predictor of 12-month all-cause mortality was STS (per 1 percent) - HR (95% CI) 1.130 (1.038 to 1.231); $p = 0.05$.

DISCUSSION

The study shows that (1) in the era of TAVI/AVR, BAV gains new important indication for bridging high-risk patients with severe AS, at first not suitable for definitive therapy, (2) BAV is an acceptable palliative treatment for patients with contraindication for TAVI/AVR and/or with expected short survival in relieving their symptoms, (3) BAV is important procedure in bridging patients for noncardiac surgeries, (4) BAV can lead to improvement of LVEF which may have impact on further definitive treatment and prognosis after that treatment.

We report favorable results of 114 performed BAVs with improvement of AV hemodynamic parameters, LVEF and acceptable rate of complications. Women account for more than half of study population which is rather similar to reported in other studies on the treatment of AS with BAV or TAVI [11].

Achieved procedural increase in AVA was 0.23 cm^2, decrease in mean and peak gradient was 17.5 mm Hg and 28.6 mm Hg, that is consistent with other reports from BAV studies [12–18]. These effects has not reached baseline parameters in 1, 6, 12 months follow-up which emphasizes BAV effectiveness, however AVA had tendency to decrease and transaortic gradients were gradually increasing to the end of observation period. This highlights the recurrence of AS severity and symptoms with passing time from BAV. Significant increase in LVEF was also confirmed in short-term and long-term follow-up after TAVI, especially in patients with severe impairment of left ventricle at baseline [15,16]. In spite of these favorable results long-term mortality remained high, especially in patients scheduled for the palliative treatment. A mortality rate of about 20% after 12 months seems acceptable given the high-risk population enrolled. Also, there are relevant rates of noncardiac death for patients after BAV, which may be related to a selection bias wherein this population is excluded from a more definite treatment due to the high number of comorbidities [17]. In multivariable analysis only STS score was identified as independent predictor of mortality. Importantly, Moretti et al. [17] have shown that reduced renal function and higher STS score may decrease the chance of undergoing definite interventions in AS, especially surgical AVR.

Major complications occurred in 21 patients with 3 procedural deaths which appears similar to the rates

showed in previous studies [6,18]. Within this we noted quite high rate of vascular complications which was already reported [5] and is mostly related to the use of large arterial sheaths, peripheral arterial disease and in patients without vascular closure devices. On the other hand, these rates were two-times lower than reported for TAVI [4]. Periprocedural deaths were in fact limited to patients with hemodynamic instability/cardiogenic shock before procedure. In contrast to previous reports [6,19,20], we did not observed stroke, myocardial infarction, and other major complications of BAV.

Our observations are consistent with other studies confirming resurgence of BAV in the era of TAVI [13,17,20]. Its use as a bridge gives opportunity to improve the clinical and hemodynamic response among treated patients. This effect can be crucial in decision making and planning further treatment with TAVI/AVR, especially when there are serious comorbidities, extreme frailty or very low ejection fraction. In natural history of nonsurgically treated severe AS during long-term follow-up more significant decrease in AVA and increase of pulmonary artery systolic pressure correlate with lower reduction of LVEF [21]. This fact may suggest that LV contractility remains resistant longer to unfavorable hemodynamics caused by deteriorating severe AS. On the other hand, a small improvement in AVA after BAV could have an impact on LVEF recovery as presumably it is more sensitive to any decrease in afterload. Taken together, this study provides additional evidence for possible improvement of initially depressed LVEF (increase by 16%) after BAV [14,[22–24]]. Those patients are more desirable candidates for TAVI/AVR and this may confirm actual important role of BAV. However, taking into account the gradual deterioration of valve parameters and persistent high risk of death, "watchful waiting strategy" should be preferred over routine follow-up after BAV. Only half of patients (51.1%) finally bridged to TAVI reached the procedure due to new concomitant comorbidities, still limited access to TAVI and withdrawal of consent after improvement of symptoms. These results are consistent with recent multicenter registry of patients undergoing BAV [17].

This study has several limitations. First, the size of the study group was rather small. Second, it is prospective, nonrandomized two-center study. Third, the completeness of observations after BAV was limited as some patients were treated with definitive therapy and/or could not come for an out-patients visit. Fourth, survival rate could be influenced not only by valvular disease but presumably also by severe comorbidities. Finally, some may explain the rise in LVEF in patients with a low baseline LVEF by the regression to the mean phenomenon.

CONCLUSIONS

BAV is a useful procedure in high-risk severe AS patients, nevertheless limited by long-term outcomes. Limitations concern intermittent improvement of symptoms, AVA, pAVG, and mAVG, however achieved effects can be sufficient in bridging patients for TAVI/AVR. Our study provides additional evidence that BAV in some patients result in recovery of initially depressed LVEF (<40%) which may lead to subsequent evaluation of patients risk may result in final qualification for TAVI/AVR. BAV in patients not suitable for TAVI/AVR is considered as a last option of treatment with benefits of symptomatic relief and/or improving mobility.

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ORIGINAL INVESTIGATION

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In-hospital and long-term outcomes of percutaneous balloon aortic valvuloplasty with concomitant percutaneous coronary intervention in patients with severe aortic stenosis

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Background: Severe aortic stenosis (AS) often coexists with significant coronary artery disease.

Objective: To evaluate procedural complications and long-term outcomes of patients with severe AS undergoing balloon aortic valvuloplasty (BAV) and percutaneous coronary intervention (PCI).

Methods: A total of 97 patients with severe AS underwent 104 BAVs as palliative procedure, bridge to definitive treatment, or before urgent non-cardiac surgery. Patients were followed-up for at least 12 months.

Results: Of the 97 patients, 34 (35.0%) underwent standalone BAV, 45 (46.4%) underwent BAV with coronary angiography, and 18 (18.6%) BAV with PCI. There were no differences in baseline characteristics and indications for BAV among the groups ($P > 0.05$). No higher risk of complications after BAV performed with concomitant coronary angiography/PCI was observed. Transcatheter aortic valve implantation was performed after BAV in 13 (13.4%) patients and surgical aortic valve replacement in three (3.1%) patients. In spite of no difference in in-hospital mortality (5.6% vs. 8.9%; $P = 0.76$), patients with BAV and concomitant PCI had lower long-term mortality than patients with BAV and concomitant coronary angiography (28.5% vs. 51.0%; $P = 0.03$). In multivariable Cox analysis adjusted for age, sex, and body mass index, the Society of Thoracic Surgeons Predicted Risk of Mortality score was identified as the only independent predictor of long-term mortality for all patients (HR: 1.09, 95%CI: 1.04-1.15, $P = 0.0006$).

Conclusions: Concomitant PCI or coronary angiography performed with BAV may not increase the risk of major and vascular complications. Patients with BAV and concomitant PCI may have better survival than patients with BAV and concomitant coronary angiography.

KEYWORDS
angioplasty, aortic stenosis, balloon aortic valvuloplasty, coronary artery disease, revascularization

1 | INTRODUCTION

Frequent coexistence of coronary artery disease (CAD) and valvular disease especially among elderly patients makes the planning of a combined definitive treatment more difficult. Interestingly, etiology of degenerative calcific aortic stenosis (AS) is similar to the etiology of CAD with arteriosclerotic, inflammatory and calcific processes.[1] Therefore, in almost half of the patients with AS >70 years of age, valvular disease coexists with CAD.[2] The current European Society of Cardiology (ESC) guidelines recommend coronary angiography before valvular heart surgery in case of any of the following: history of CAD, suspected myocardial ischemia, left ventricular systolic dysfunction, in men >40 years and postmenopausal women, or patients with ≥1 cardiovascular risk factor (Class I, Level C).[3] In patients with a primary indication for aortic/mitral valve surgery, coronary artery bypass grafting (CABG) remains the preferred treatment if coronary artery diameter stenosis is ≥70% (Class I, Level C).[3] Until recently, the standard treatment option for patients with severe AS and CAD has been surgical aortic valve replacement (AVR) with CABG. After the introduction of transcatheter aortic valve implantation (TAVI), new combined models of treatment are being developed with additional use of percutaneous coronary intervention (PCI) and/or balloon aortic valvuloplasty (BAV) if needed.[4–15] The previous studies have confirmed that PCI is feasible and safe in selected high-risk or inoperable patients with symptomatic severe AS.[4,12,16] For patients scheduled for TAVI, the most frequent approach to treat coexisting CAD is staged PCI typically performed a few weeks before TAVI.[13] On the other hand, concomitant PCI and TAVI has also been shown to be feasible.[6,11,13] Similarly, patients with significant CAD scheduled for BAV can be treated with PCI at the time of BAV (as a single procedure) or staged PCI.[9,17] However, data on the safety of BAV with concomitant PCI are scarce. Thus, we sought to assess the safety and outcomes of BAV and concomitant coronary angiography/PCI in high-risk patients who could not be treated at the time with either TAVI or AVR with CABG.

2 | METHODS

2.1 | Patients and data collection

We included 97 consecutive patients with severe symptomatic AS (aortic valve area [AVA] <1 cm^2, indexed AVA <0.6 cm^2/m^2 body surface area) who underwent 104 BAVs between December 2013 and March 2017 in a single Polish center experienced in diagnostics and interventional treatment of both AS and CAD. All patients were qualified for BAV or coronary angiography with BAV by an interdisciplinary team of specialists (heart team). The only contraindication for BAV was a baseline severe aortic regurgitation (AR) determined by transthoracic echocardiography. PCI was performed in patients presenting with unstable angina (UA), non ST-segment elevation myocardial infarction (NSTEMI), and stable angina with angiographically significant coronary artery stenoses. Coronary angiography was not repeated if the patient had known coronary anatomy (procedure within the last 6 months) and had no history of previous PCI. The study was approved by the institutional review board and all eligible patients signed the informed consent. Data were collected prospectively. The procedural risk was estimated by the logistic European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) and the Society of Thoracic Surgeons Predicted Risk of Mortality (STS) score.

2.2 | Procedure

Coronary angiography/PCI was guided by fluoroscopy. The same femoral retrograde approach was used in case of concomitant coronary angiography/PCI and then during BAV to reach in aortic valve under echocardiographic and fluoroscopic guidance. BAV was proceeded once the coronary anatomy was known and hemodynamically significant lesions were treated with stent(s). Patients with concomitant PCI were given a 600-mg clopidogrel loading dose during the procedure. Balloon sizing was guided by the echocardiographic measurement of the aortic valve annulus. Exact positioning of the balloon during BAV was obtained by rapid ventricular pacing. Vascular accesses were closed with Angio-Seal vascular closure device (St. Jude Medical, St. Paul, MN) or with manual compression. No concomitant use of cardiac support devices was required during the procedure. In-hospital major complications were defined as severe AR, cardiac tamponade, the need for permanent pacemaker implantation, stroke, myocardial infarction, pulmonary edema, acute limb ischemia, and serious vascular complications requiring intervention and/or transfusion. Baseline and procedural characteristics, as well as long-term outcomes, were assessed in three groups—standalone BAV, BAV with coronary angiography (only), and BAV combined with PCI. Patients were followed up for at least 12 months or until the occurrence of repeated BAV, definitive treatment (TAVI/AVR), or death.

2.3 | Echocardiographic data

Pre-, post-BAV, and 1-, 6-, 12-month follow-up echocardiograms were performed by the same experienced echocardiographers using measurements of AVA (continuity equation), peak (pAVG) and mean (mAVG) AV gradients, degree of AR, and left ventricular ejection fraction (LVEF) were based on M-mode, doppler, and two-dimensional conventional echocardiography.[3] Echocardiographic data were presented and assessed for patients undergoing standalone BAV and BAV with coronary angiography or PCI.

2.4 | Statistical methods

Continuous variables were expressed as mean (±SD) or median (IQR or minimum/maximum value). The Shapiro-Wilk test was used to determine normal distribution. Continuous variables were compared between two groups using the unpaired or paired Student's *t*-test when normally distributed and the Mann-Whitney *U*-test or Wilcoxon signed-rank test when not normally distributed, as appropriate. Among three groups, means were compared by univariate ANOVA followed by Tukey's test and medians were compared by Kruskal-Wallis test for multiple comparisons. Homogeneity of variance

was checked using Cochran's test. Categorical variables were expressed as number (percentage) and analyzed using the Pearson's χ^2 test or Fisher's exact test, as appropriate. Kaplan-Meier survival curves were constructed and compared by the log-rank test. Univariate Cox regression analysis was performed on each of the variables to estimate the hazard ratio and 95% confidence interval. Multivariable Cox regression analysis was performed to identify the independent predictors of long-term mortality with potential confounders locked in the models. A two-sided *P*-value <0.05 was considered statistically significant. Statistical analyses were performed with STATISTICA version 13 (Statsoft, Inc., Tulsa, OK).

3 | RESULTS

3.1 | Baseline characteristics

Data on 97 patients with severe symptomatic AS undergoing BAV were collected. Of those, 34 patients (35.0%) underwent standalone

TABLE 1 Baseline characteristics

Variable	BAV (*n* = 34)	BAV+angiography (*n* = 45)	BAV+PCI (*n* = 18)	*P*	BAV+angiography/PCI (*n* = 63)	*P*
Age (years)	83.9 ± 5.6	84.6 ± 5.4	86.1 ± 3.4	0.37	85.0 ± 5.0	0.32
Sex (men)	25 (73.5)	25 (55.6)	4 (22.2)	0.12	39 (61.9)	0.25
BMI (kg/m^2)	26.7 ± 5.7	28.1 ± 6.7	23.5 ± 2.3	0.06	26.7 ± 6.1	0.98
Euroscore II (%)	8.1 (22.2-30.0)	8.2 (5.4-10.8)	8.3 (5.0-15.3)	0.78	8.3 (5.0-11.8)	0.63
STS score (%)	7.5 (5.4-11.0)	7.9 (5.8-10.7)	8.6 (7.1-11.9)	0.64	8.2 (6.0-11.2)	0.45
Arterial hypertension, *n* (%)	30 (88.2)	47 (82.2)	18 (88.9)	0.68	53 (84.1)	0.41
Diabetes mellitus, *n* (%)	12 (35.3)	17 (37.8)	6 (33.3)	0.93	23 (36.5)	0.91
Coronary artery disease, *n* (%)	29 (85.3)	35 (77.9)	18 (100.0)	0.08	53 (84.1)	0.88
Previous myocardial infarction, *n* (%)	13 (38.2)	17 (37.8)	11 (61.1)	0.20	28 (44.4)	0.56
Previous PCI, *n* (%)	7 (20.6)	14 (31.1)	8 (44.4)	0.20	22 (34.9)	0.14
Previous CABG, *n* (%)	0 (0.0)	4 (8.9)	1 (5.6)	0.20	5 (7.9)	0.11
Previous BAV, *n* (%)	5 (71.4)	2 (28.6)	0 (0.0)	0.09	2 (28.6)	0.35
Previous cerebrovascular events, *n* (%)	4 (11.8)	8 (17.8)	2 (11.1)	0.68	10 (15.9)	0.41
Atrial fibrillation, *n* (%)	18 (52.9)	24 (53.3)	7 (38.9)	0.54	31 (49.2)	0.72
Peripheral vascular disease, *n* (%)	7 (20.6)	6 (13.3)	2 (11.1)	0.58	8 (12.7)	0.30
Previous peripheral arteries intervention, *n* (%)	1 (2.9)	3 (6.7)	0 (0.0)	0.44	3 (4.7)	0.57
Chronic kidney disease, *n* (%)	20 (58.8)	25 (55.6)	12 (66.7)	0.72	37 (58.7)	0.99
COPD/asthma, *n* (%)	5 (14.7)	7 (15.6)	2 (11.1)	0.90	9 (14.3)	0.96
Neoplasm, *n* (%)	1 (2.9)	5 (11.4)	0 (0.0)	0.14	5 (8.1)	0.30
Previous radiotherapy, *n* (%)	0 (0)	3 (6.7)	0 (0.0)	0.17	3 (4.8)	0.27
Porcelain aorta, *n* (%)	1 (2.9)	0 (0.0)	1 (5.6)	0.33	1 (1.6)	0.58
Presenting symptoms						
NYHA class I, *n* (%)	1 (2.9)	0 (0.0)	0 (0.0)	0.45	0 (0.0)	0.27
NYHA class II, *n* (%)	2 (5.9)	2 (4.4)	2 (11.1)		4 (6.3)	
NYHA class III, *n* (%)	13 (38.2)	13 (28.9)	3 (16.7)		16 (25.4)	
NYHA class IV, *n* (%)	18 (52.9)	30 (66.7)	13 (72.2)		43 (68.2)	
CCS class I, *n* (%)	18 (62.1)	22 (59.5)	10 (55.6)	0.60	32 (58.2)	0.69
CCS class II, *n* (%)	5 (17.2)	5 (13.5)	1 (5.6)		6 (10.9)	
CCS class III, *n* (%)	5 (17.2)	8 (21.6)	7 (38.9)		15 (27.3)	
CCS class IV, *n* (%)	1 (3.4)	2 (5.4)	0 (0.0)		2 (3.7)	
Syncope, *n* (%)	4 (11.8)	8 (18.2)	2 (11.1)	0.65	10 (16.1)	0.40
Cardiogenic shock, *n* (%)	1 (2.9)	3 (6.7)	0 (0.0)	0.44	3 (4.7)	0.56

Data are number (percentage), median (interquartile range), or mean ± standard deviation. BMI, body mass index; CABG, coronary artery bypass graft surgery; CCS, Canadian Cardiovascular Society functional class; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association functional class; PCI, percutaneous coronary interventions; STS, Society of Thoracic Surgeons Predicted Risk of Mortality.

TABLE 2 Indications for BAV and received definitive treatment

Variable	BAV (*n* = 34)	BAV+angiography (*n* = 45)	BAV+PCI (*n* = 18)	*P*	BAV+angiography/PCI (*n* = 63)	*P*
Bridge for TAVI	22 (64.7)	21 (46.7)	9 (50.0)	0.27	30 (47.6)	0.10
Bridge for AVR	0 (0.0)	0 (0.0)	0 (0.0)	–	0 (0.0)	–
Palliation	9 (26.5)	17 (37.8)	9 (50.0)	0.23	26 (41.2)	0.14
Cardiogenic shock	1 (2.9)	3 (6.7)	0 (0.0)	0.44	3 (4.8)	0.67
Non-cardiac surgery	2 (5.9)	4 (8.9)	0 (0.0)	0.41	4 (6.4)	0.92
Received TAVI	4 (11.7)	5 (11.1)	4 (22.2)	0.48	9 (14.3)	0.72
Received AVR	2 (5.9)	1 (1.6)	0 (0.0)	0.45	1 (1.6)	0.25
Duration of follow-up, *n* (days)	355 (131-705)	228 (62-415)	377 (142-739)	0.47	295 (72-472)	0.27

BAV, 45 (46.4%) underwent BAV with coronary angiography, and 18 (18.6%) underwent BAV with PCI. In our center, BAV was performed with the intention of bridge for TAVI, bridge for AVR, as a palliative procedure, a rescue procedure for cardiogenic shock, or before urgent non-cardiac surgery. Seven patients underwent re-BAV. There were no differences in baseline characteristics, comorbidities, and presentation among the groups (Table 1). Similarly, no differences between the three groups in indications and definitive treatment received were observed (Table 2). Almost half of the patients who underwent BAV with PCI had a history of previous PCI. BAV was performed with PCI in 18 (18.6%) patients of whom 15 (83.3%) patients had one-vessel disease, one (5.6%) patient had two-vessel disease without left main involvement, and two (11.1%) patients had left main artery stenosis with one-vessel and two-vessel disease, respectively. Within this group, on admission, two patients presented with NSTEMI, three patients with UA, and the remaining patients presented with the symptoms of stable angina.

3.2 | Procedural data

Detailed procedural data stratified by performed procedures are shown in Table 3. A higher contrast load, radiation dose, and longer fluoroscopy time in patients with concomitant PCI or coronary angiography were noted.

TABLE 3 Procedural data

Variable	BAV (*n* = 34)	BAV +angiography (*n* = 45)	BAV+PCI (*n* = 18)	*P*	BAV+angiography/ PCI (*n* = 63)	*P*
Balloon size (mm)	22 (20-22)	22 (20-24)	20 (22-24)	0.72	22 (20-22)	0.43
Number of inflations, (*n*)	2 (2-2)	2 (1-2)	2 (1-2)	0.84	2 (1-2)	0.94
Size for femoral approach (F)	9 (9-9)	9 (9-10)	9 (9-10)	0.96	9 (9-10)	0.78
Heparin dose (IU)	4703 ± 1501	4587 ± 1041	5833 ± 1294*	0.02	4967 ± 1254*	0.57
Fluoroscopic time (min)	6.4 (4.3-10.0)	10.4 (6.5-20.9)	18 (10-22)*,**	0.0005	10.5 (6.6-17.7)*	0.002
Radiation dose (Gy)	0.16 (0.08-0.29)	0.36 (0.27-0.50)*	0.66 (0.50-0.88)*	<0.0001	0.45 (0.3-0.67)*	<0.0001
Contrast media volume (mL)	0 (0-50)	100 (50-100)*	150 (50-200)*	<0.0001	100 (50-130)*	<0.0001
Vascular closure device, *n* (%)	4 (12.5)	4 (8.9)	1 (5.6)	0.71	5 (7.9)	0.47
Average length of hospital stay (days)	11 (9-14)	9 (8-14)	9 (7-13)	0.30	9 (8-14)	0.12
Hemoglobin before BAV (g/dL)	11.8 ± 1.3	12.0 ± 1.3	11.8 ± 1.7	0.77	11.9 ± 1.4	0.61
Hemoglobin after BAV (g/dL)	10.7 ± 1.7	10.8 ± 1.8	10.3 ± 1.8	0.60	10.7 ± 1.8	0.98
Hematocrit before BAV (%)	35.5 ± 3.5	36.4 ± 3.7	35.8 ± 4.7	0.55	36.2 ± 4.0	0.37
Hematocrit after BAV (%)	32.3 ± 4.8	33.3 ± 5.4	31.4 ± 4.9	0.40	32.7 ± 5.3	0.79
Creatinine before BAV (μmol/L)	97 (84-117)	97 (79-118)	86 (76-119)	0.41	94 (78-118)	0.12
Creatinine after BAV (μmol/L)	101 (87-127)	107 (94-143)	116 (86-154)	0.63	111 (90-143)	0.42
25% creatinine increase after BAV, *n* (%)	7 (22.6)	10 (25.0)	7 (38.7)	0.44	17 (29.3)	0.50

*$P < 0.05$ compared with BAV.
**$P < 0.05$ compared with BAV+angiography.

TABLE 4 Echocardiographic data before and after BAV and at 1, 6, 12-month follow up

Variable		Baseline	After BAV	1 month	6 months	12 months
AVA (cm^2)	BAV	0.51 ± 0.03 *n* = 34	0.70 ± 0.04* *n* = 21	0.71 ± 0.04* *n* = 20	0.63 ± 0.05 *n* = 15	0.73 ± 0.08# *n* = 5
	BAV +angiography/PCI	0.53 ± 0.02 *n* = 58	0.75 ± 0.02* *n* = 43	0.70 ± 0.03* *n* = 34	0.56 ± 0.04 *n* = 13	0.50 ± 0.07 *n* = 4
pAVG (mmHg)	BAV	95.6 ± 5.4 *n* = 32	68.2 ± 6.4* *n* = 23	72,7 ± 6.8* *n* = 20	83.3 ± 7.7 *n* = 16	92 ± 13.7 *n* = 5
	BAV +angiography/PCI	88.2 ± 3.4 *n* = 59	69.1 ± 3.4* *n* = 55	69.4 ± 4.4* *n* = 34	90.5 ± 6.9 *n* = 14	85.8 ± 12.8 *n* = 4
mAVG (mmHg)	BAV	59.0 ± 3.6 *n* = 33	43.3 ± 4.4 *n* = 22	45.8 ± 4.6 *n* = 20	51.8 ± 5.1 *n* = 16	62.2 ± 9.2 *n* = 5
	BAV +angiography/PCI	56.4 ± 2.4 *n* = 58	43.4 ± 2.7* *n* = 46	47.0 ± 3.1 *n* = 34	60.0 ± 5.0 *n* = 13	57.2 ± 9.1 *n* = 4
LVEF for all patients (%)	BAV	52 (40–65) *n* = 34	60 (40–65) *n* = 17	60 (38–65) *n* = 20	55 (40–63) *n* = 16	48 (45–50) *n* = 5
	BAV +angiography/PCI	50 (34–60) *n* = 62	45 (28–65) *n* = 37	60 (45–65) *n* = 34	60 (50–65) *n* = 14	65 (57–67) *n* = 4
RVSP (mmHg)	BAV	49.0 ± 3.1 *n* = 34	57 ± 6.7 *n* = 7	56 ± 4.7 *n* = 14	65 ± 5.3 *n* = 11	35 ± 17.7 *n* = 1
	BAV +angiography/PCI	46.5 ± 2.2 *n* = 62	44.7 ± 5.4 *n* = 10	56.1 ± 3.5 *n* = 24	57.8 ± 5.4 *n* = 11	60.3 ± 9.9 *n* = 1
Aortic regurgitation						
None/trivial, *n* (%)	BAV	14 (45.1)	8 (36.4)	6 (31.6)	2 (40.0)	2 (40.0)
	BAV +angiography/PCI	20 (35.7)	9 (21.6)	6 (18.1)	0 (0.0)	0 (0.0)
Mild, *n* (%)	BAV	16 (51.6)	9 (40.9)	12 (63.1)	3 (60.0)	3 (60.0)
	BAV +angiography/PCI	33 (58.9)	26 (63.4)	24 (72.7)	3 (75.0)	3 (75.0)
Moderate, *n* (%)	BAV	1 (3.2)	5 (22.7)	1 (5.2)	0 (0.0)	0 (0.0)
	BAV +angiography/PCI	3 (5.3)	6 (14.6)	3 (9.1)	1 (25.0)	1 (25.0)
Severe, *n* (%)	BAV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	BAV +angiography/PCI	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

*$P < 0.05$ compared with baseline, #$P < 0.05$ BAV vs BAV + angiography/PCI.
LVEF, denotes left ventricular ejection fraction; AVA, aortic valve area; pAVG, peak aortic valve gradient, mAVG, mean aortic valve gradient, RVSP, right ventricular systolic pressure.
Data are number (percentage), median (interquartile range) or mean ± standard deviation.

3.3 | Echocardiographic data

Echocardiographic data are summarized in Table 4. Both patients from the standalone BAV group and BAV with coronary angiography/PCI group were characterized by increased AVA after BAV in comparison to baseline, which remained significant only directly post-BAV and at 1-month follow-up (BAV: +0.19, +0.20 cm^2, BAV +coronary angiography/PCI: +0.22, +0.17 cm^2, respectively; $P < 0.05$ for all). Moreover in both groups, a decrease in pAVG directly after BAV and at 1-month follow-up was observed (BAV −27.4, −22.9 mmHg, BAV+coronary angiography/PCI −19.1, −18.8 mmHg, respectively; $P < 0.05$ for all). In all patients with baseline LVEF <40% ($n = 15$), an increase in LVEF after 1 month was confirmed (+25.5%; $P = 0.01$).

3.4 | BAV complications and mortality

No difference in the length of hospital stay was observed ($P = 0.12$). Occurrence of major complications and in-hospital mortality did not predominate in the group with BAV and PCI/coronary angiography versus BAV alone (12.7% vs. 14.7%; $P = 0.51$; 7.9% vs. 11.8%; $P = 0.39$; Table 5). Cardiac tamponade was observed in four (4.1%) patients (in two, it was fatal). In addition, the occurrence of one (1.0%) acute limb ischemia, one (1.0%) need for permanent pacemaker implantation, and one (1.0%) pulmonary edema was confirmed. None of the complications were treated with emergency cardiac or vascular surgery. No cases of stroke or myocardial infarction after BAV were observed. Combining BAV and coronary angiography/PCI did not increase the prevalence of vascular or bleeding complications ($P > 0.05$) especially given the fact

TABLE 5 In-hospital major and vascular access complications

Variable	BAV (*n* = 34)	BAV+angiography (*n* = 45)	BAV+PCI (*n* = 18)	*P*	BAV+angiography/PCI (*n* = 63)	*P*
Major complications, *n* (%)	5 (14.7)	7 (15.6)	1 (5.6)	0.55	8 (12.7)	0.51
In-hospital mortality, *n* (%)	4 (11.8)	4 (8.9)	1 (5.6)	0.76	5 (7.9)	0.39
Tamponade, *n* (%)	2 (5.9)	2 (4.4)	0 (0.0)	0.59	2 (3.2)	0.44
Permanent pacemaker implantation, *n* (%)	0 (0.0)	1 (2.2)	0 (0.0)	0.56	1 (1.6)	0.65
Acute lower limb ischemia, *n* (%)	0 (0.0)	1 (2.2)	0 (0.0)	0.56	1 (1.6)	0.65
Pulmonary edema, *n* (%)	1 (2.9)	0 (0.0)	0 (0.0)	0.39	0 (0.0)	0.35
Need for red blood cells transfusion, *n* (%)	1 (3.0)	4 (8.8)	1 (5.6)	0.54	5 (7.9)	0.31
1 unit, *n* (%)	0 (0.0)	2 (4.4)	0 (0.0)	0.31	2 (3.2)	0.42
≥2 units, *n* (%)	1 (3.0)	2 (4.4)	1 (5.6)	0.90	3 (4.8)	0.56
Vascular access site complications, *n* (%)	5 (14.7)	4 (8.9)	1 (5.6)	0.53	5 (7.8)	0.23
Pseudoaneurysm, *n* (%)	3 (8.8)	4 (8.9)	0 (0.0)	0.42	4 (6.3)	0.48
Hematoma, *n* (%)	2 (5.9)	0 (0.0)	1 (5.6)	0.26	1 (1.6)	0.28

that antiplatelet drugs and larger doses of heparin ($P = 0.02$) were used with PCI. During median follow-up of 237 (63–405) days, 16 (16.5%) patients received TAVI/AVR as their definitive treatment. In spite of no difference in in-hospital mortality (1.0% vs. 8.9%; $P = 0.76$), patients with BAV and concomitant PCI had lower mortality than patients with BAV and concomitant coronary angiography at 12 months (28.5% vs. 51.0%; $P = 0.03$). In multivariable Cox analysis adjusted for age, sex, and body mass index, STS score was identified as the only independent predictor of long-term mortality for all the patients (HR: 1.09, 95%CI: 1.04–1.15, $P = 0.0006$). Kaplan-Meier survival curves for patients with BAV with coronary angiography and BAV with PCI confirmed higher survival in patients with BAV and PCI (Figures 1 and 2; log-rank test, $P = 0.03$).

4 | DISCUSSION

The most important finding of this study is that patients with BAV and concomitant PCI had higher survival rates compared to patients with BAV and concomitant coronary angiography. Furthermore, our study shows that BAV performed with concomitant coronary angiography/PCI does not increase procedural complications, in-hospital and long-term mortality, and does not prolong the hospital stay. It may suggest that BAV with PCI as an approach of treating severe AS with coexisting significant CAD is not associated with additional risk. According to the ESC Guidelines, patients with severe AS and concomitant CAD should preferably be treated with CABG with AVR. However, many of them do not qualify for surgical treatment due to comorbidities or high procedural risk and even if they do so, the incidence of periprocedural complications remains very high.[18,19] In the era of TAVI-staged treatment with first PCI and then TAVI may be available for patients who are ineligible for concomitant CABG and AVR. Additionally, one-stage approach of concomitant PCI and TAVI was shown to be feasible and safe.[16] Therefore, BAV with PCI may also be a feasible and convenient option of treatment in a particular group of patients with severe AS with CAD and contraindications for surgical treatment.

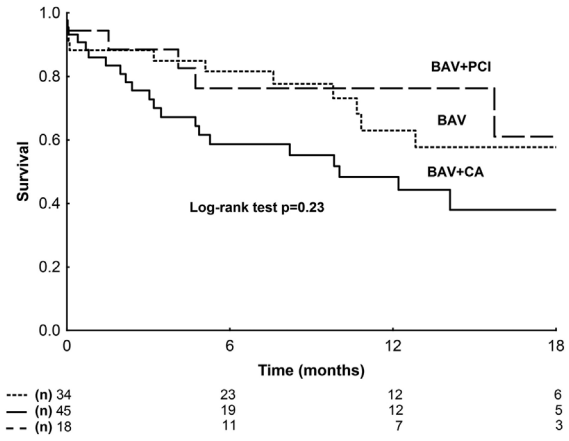

FIGURE 1 Kaplan-Meier curve for overall survival according to treatment method: balloon aortic valvuloplasty (BAV), BAV +coronary angiography (CA), and BAV+percutaneous coronary intervention (PCI)

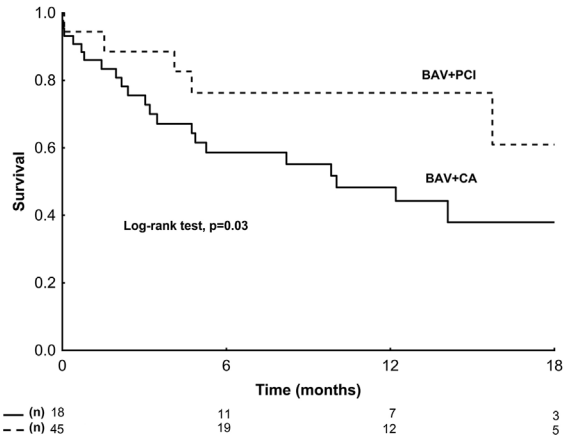

FIGURE 2 Kaplan-Meier curve for overall survival according to treatment method: BAV+coronary angiography (CA) and BAV +percutaneous coronary intervention (PCI)

The knowledge of coronary anatomy before any BAV is crucial because the rapid ventricular pacing during the procedure leads to blood pressure drop in the aorta followed by the reduction of coronary artery flow. In the case of significant coronary artery stenoses, this phenomenon can lead to peri-procedural myocardial infarction and/or hemodynamic instability. Importantly, no peri-procedural myocardial infarction was observed in our study. Moreover, the same femoral retrograde approach for both procedures diminishes the risk of injury of another major artery and the need of additional immobilization of the patient, if performed separately. The amount of contrast used for the BAV alone is very limited, as it serves mainly to prepare the aortic balloon. Therefore, observed higher amount of used contrast resulted from concomitant coronary angiography/PCI. Nevertheless, none of those patients suffered from contrast-induced nephropathy, which might suggest appropriateness of this strategy also in patients with renal impairment.

A coronary evaluation is recommended before valvular heart surgery as both conditions severe AS and CAD can cause chest pain and dyspnea with different predominance of symptoms. Importantly, about half of the patients with severe AS have concomitant significant CAD.[20] Furthermore, patients with severe AS tend to minimize physical exertion to prevent the occurrence of symptoms, which makes the patient's medical history of limited use. Symptomatic or asymptomatic clinical presentation of a patient with severe AS is therefore a poor diagnostic tool to predict presence of CAD.[16]

Impaired LVEF in severe AS with CAD may result from both conditions.[21–24] Our study showed the improvement of LVEF in the group of patients with LVEF <40% after 1 month from the procedure (BAV/PCI/coronary angiography). We did not manage to prove this phenomenon in the group of patients who underwent BAV and PCI which was probably due to a small sample size. However, in many previous studies both procedures were shown to separately contribute to the improvement of LVEF.[25–27] Despite the lack of statistical significance, our study suggests that coronary revascularization can magnify effect of BAV on LVEF improvement and further results in a higher survival. In line with our results, the latest and largest registry of 2127 procedures from hospitals in the United States comparing BAV versus BAV with PCI has also reported no difference in in-hospital mortality, length of hospital stay, and procedural complications. On the other hand, we reported lower percentage of complications and in-hospital mortality in the group with BAV and PCI with no differences in baseline characteristics contrary to higher prevalence of hypertension, diabetes, peripheral vascular disease, anemia, or coagulopathy in the group with BAV and PCI reported by Singh et al.[17] Particular attention should be given to our study as we provided data not only for in-hospital but also 12-month follow-up that showed higher survival in the group of patients with BAV and PCI. This suggests that combining both procedures, if needed, might lead to significant profits with acceptable procedural risk.

4.1 | Study limitations

Our study has several limitations. This was an observational, single-center study, therefore some degree of bias cannot be excluded. The smaller number of patients with BAV and PCI than with coronary angiography could have influenced the results. Due to a relatively small number of patients with LVEF <40% who underwent BAV with PCI, we were not able to confirm the presence of the relationship between LVEF improvement and the higher survival rates. The lack of follow-up echocardiograms in some of the patients after BAV resulted from difficulties in attending outpatient visits. Thus, our results should be considered exploratory and hypothesis-generating. Further studies specifically on concomitant use of BAV and PCI are needed to validate our observations.

5 | CONCLUSIONS

Concomitant PCI or coronary angiography performed with BAV may not increase the risk of major and vascular complications of BAV. Patients with BAV and concomitant PCI may have better survival than patients with BAV and concomitant coronary angiography. However, these results should be confirmed in further randomized trials.

AUTHORSHIP DECLARATION

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

DISCLOSURES

The authors have no conflicts of interest to declare.

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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Impact of post-dilatation on the reduction of paravalvular leak and mortality after transcatheter aortic valve implantation

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Abstract

Background: Post-implantation paravalvular leak (PVL) remains a significant complication of transcatheter aortic valve implantation (TAVI). More importantly, its occurrence may impact long-term mortality.

Aim: We sought to evaluate the effects of balloon post-dilatation (PD) on the reduction of PVL and mortality in patients undergoing TAVI.

Methods: A total of 101 consecutive patients undergoing TAVI were enrolled. Angiography, echocardiography, and the aortic regurgitation index (ARI) were used to assess the severity of PVL before and after balloon PD. Patients were divided into two groups based whether or not PD after TAVI was performed. Reduction of PVL, change of ARI, and clinical outcomes were assessed.

Results: Balloon post-dilatation was performed in 23 (22.8%) patients. In 95.6%, PVL reduction was successful (no or mild PVL). PD increased the ARI from 23.4% (22.4–24.0) to 27.1% (26.1–28.3); $p < 0.001$. Thirty-day mortality rate was 14.1% in the PD (–) group vs. 0.0% in the PD (+) group; $p = 0.07$. One-year mortality (21.8% vs. 4.3%, $p = 0.97$) and procedural stroke rate (7.7% vs. 8.7%, $p = 0.99$) were not different between the groups.

Conclusions: Balloon post-dilatation may be a safe and effective technique to reduce moderate to severe PVL after TAVI.

Key words: aortic stenosis, transcatheter aortic valve implantation, paravalvular leak, post-dilatation

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INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is a less invasive treatment option for elderly, high-risk patients with symptomatic severe aortic stenosis (AS) than surgical aortic valve replacement. TAVI improves survival and quality of life in inoperable patients as compared to medical treatment of severe AS [1–3]. However, post-implantation paravalvular leak (PVL) remains a significant TAVI-related complication [4]. Importantly, the presence of PVL may worsen clinical outcomes of patients undergoing TAVI [5]. It is present in up to 70% of all patients undergoing TAVI, and more than mild PVL has been reported in about 10–15% of all TAVI patients [1, 6–14]. Angiography and echocardiography are useful tools to quantify the degree of PVL immediately after deployment of the prosthesis and can be used to identify patients who might benefit from optimisation techniques. Combining invasive haemodynamic measurements with assessment of the aortic regurgitation index (ARI) and imaging may be even more accurate than imaging alone [9, 15, 16]. Balloon post-dilatation (PD) can reduce PVL by achieving a better expansion of the prosthesis and optimal sealing of the paravalvular space. Valve-in-valve implantation is another option to overcome significant PVL, especially if the implantation position is more deep or more shallow than expected [17–19]. However, data on the impact of PD on long-term outcomes after TAVI are scarce. The aim of our study was to evaluate whether balloon PD is safe and effective in reducing PVL after TAVI and to assess its impact on mortality.

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METHODS

A total of 101 consecutive high-risk elderly patients with severe symptomatic AS undergoing TAVI were enrolled between November 2008 and November 2014. Patient screening and selection was performed by a multidisciplinary Heart Team supported by clinical and imaging resources. TAVI procedures were performed using Edwards Sapien, Edwards Sapien XT, Edwards Sapien 3 (Edwards Lifesciences, Irvine, USA) Medtronic Corevalve, EvolutR (Medtronic Inc., Minneapolis, USA), and JenaValve (JenaValve Technology, Munich, Germany). Access routes were transfemoral, transapical, and direct aortic. Procedures were performed under general anaesthesia or sedation. Balloon aortic valvuloplasty was performed in each case. Baseline characteristics, and procedural and outcomes data was collected and analysed prospectively. After valve deployment, the degree of PVL was routinely assessed by aortic root angiography (30 mL contrast dye at a flow rate of 15 mL/s) according to the visually estimated density of opacification of the left ventricle (LV) into three degrees adapted from the VARC-2 criteria: mild (reflow of contrast in the outflow tract and middle portion of the LV but clearing with each beat), moderate (reflow of contrast in the whole LV cavity with incomplete washout in a single beat and faint opacification of the entire LV over several cardiac cycles), and severe (opacification of the entire LV with the same intensity as in the aorta and persistence of the contrast after a single beat) and with echocardiography [20]. In all patients, a 6 Fr pigtail catheter was placed approximately 2 cm above the aortic valve. In all patients, haemodynamics were assessed and calculation of the ARI was performed to quantify the extent of PVL more precisely and to have a point of reference before PD was carried out. The ARI was calculated according to the following formula: ([diastolic blood pressure – left ventricular end-diastolic pressure]/systolic blood pressure) × 100%, from 5 to 10 min after valve deployment or PD. A detailed description of ARI assessment and its limitations were described previously [9]. In patients with more than mild angiographically detected PVL and/or an ARI < 25%, PVL was evaluated by echocardiography, preferably transesophageal echocardiography, and if confirmed, a PD was performed. In patients with suboptimal frame expansion causing more than mild PVL, PD was performed to obtain a better expansion of the prosthesis stent frame and a better sealing of the paravalvular space. PD was performed by adding 1–2 cc of contrast dye to the delivery system of balloon expandable valves used during TAVI. For self-expandable prostheses, a 1:1 balloon to aortic native annulus was used for PD (Osypka VACS II, Osypka AG, Germany). The primary endpoint of our study was the change of the PVL grade and ARI after PD in patients undergoing TAVI. Secondary endpoints were the severity of PVL defined according to the VARC-2 criteria, all-cause mortality at 30 days and one year, and post-procedural stroke rate. Patients were divided into two groups based whether or not balloon PD after TAVI was performed. The study protocol was approved by the institutional Ethical Board.

Statistical analysis

Results are presented as numbers of patients (percentages) or the median (interquartile range [IQR]) where applicable. Differences between groups were tested using χ^2 test and the Fisher's exact test for dichotomous variables, and the Mann-Whitney U-test for continuous variables. Changes in the ARI between pre, immediately after, and post TAVI were analysed with Wilcoxon signed-rank test. Changes in the proportions of patients with none, mild, moderate, and severe PVL between pre, immediately after, and post TAVI were tested with χ^2 test. In addition, changes in the proportions of patients with "none/mild" vs. "moderate/severe" PVL were analysed using McNemar's test. The difference in mortality between patients with and without PD after TAVI during 12-month follow-up was assessed by the Kaplan-Meier method and log-rank test. All tests were two-tailed, and a p value < 0.05 was considered statistically significant. All statistical analysis was performed using SPSS 15.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

A total of 101 consecutive patients underwent TAVI. Baseline characteristics are shown in Table 1. PD was performed in 23 (22.8%) patients. Patients were divided based on the need for PD into two groups: with [PD (+), 23 patients] and without PD [PD (–), 78 patients]. Procedural data are summarised in Table 2. No annular rupture was observed in the PD (+) group. The transfemoral access was used in 73.1% of patients in the PD (–) group and in 91.3% in the PD (+) group (p < 0.001). Interestingly, the fluoroscopy time, radiation dose, and contrast medium volume were higher in patients without PD (Table 2). No difference in the size of prosthesis, annulus dimensions, and cover index between groups was found. In 95.6% of patients PVL reduction was successful (no or mild PVL). Detailed data presenting severity of PVL before and immediately after prosthesis deployment and at the end of the TAVI procedure after PD is shown in Figure 1A (for all patients) and Figure 1B (for patients requiring PD). PD increased the ARI from 23.4% (22.4–24.0) to 27.1% (26.1–28.3); p < 0.001. No coronary obstruction in the PD (+) group was noted. A trend towards increased 30-day mortality was observed in the PD (–) group (14.1% vs. 0.0%; p = 0.07). In contrast, no differences in stroke (7.7% vs. 8.7%; p = 0.99) and myocardial infarction (3.8% vs. 4.3%; p = 0.99) rates were observed. One-year mortality rate (21.8% vs. 4.3%, p = 0.07, Fig. 2) was higher in the PD (–) group, but no statistical significance was found.

We also performed a subanalysis of balloon-expandable valves (Edwards and Jena Valve) vs. self-expandable valves (Corevalve) in terms of PVL occurrence after prosthesis deployment, PD, and access site. More than mild PVL after prosthesis

Table 1. Baseline characteristics

	All patients (n = 101)	Post-dilatation (–) (n = 78)	Post-dilatation (+) (n = 23)	p
Age, median (IQR) [years]	81.0 (76.0–84.0)	81.0 (77.0–84.0)	82.0 (72.5–84.0)	0.80
Age ≥ 80 years	59 (58.4%)	46 (59.0%)	13 (56.5%)	0.83
Men	40 (39.6%)	31 (39.7%)	9 (39.1%)	0.96
Body mass index, median (IQR) [kg/m^2]	28.0 (25.2–31.1)	27.9 (25.6–30.6)	27.8 (25.6–31.3)	0.95
eGFR median, (IQR) [mL/min/1.73 m^2]	61.0 (39.0–81.0)	60.0 (43.0–76.5)	70.0 (43.5–81.0)	0.32
NYHA class:				0.019
I	0 (0.0%)	0 (0.0%)	0 (0.0%)	
II	17 (16.8%)	9 (11.5%)	8 (34.8%)	
III	74 (73.3%)	62 (79.5%)	12 (52.2%)	
IV	10 (9.9%)	7 (9.0%)	3 (13.0%)	
Arterial hypertension	94 (93.1%)	71 (91.0%)	23 (100.0%)	0.35
Diabetes mellitus	35 (34.7%)	28 (35.9%)	7 (30.4%)	0.80
Atrial fibrillation	35 (34.7%)	24 (30.8%)	11 (47.8%)	0.13
History of MI	31 (30.7%)	25 (32.1%)	6 (26.1%)	0.59
PCI	29 (28.7%)	21 (26.9%)	8 (34.8%)	0.46
CABG	17 (16.8%)	14 (17.9%)	3 (13.0%)	0.76
Chronic total occlusion	9 (8.9)	9 (11.5)	0 (0.0)	0.11
COPD	12 (11.9%)	9 (11.5%)	3 (13.0%)	0.99
Stroke/transient ischaemic attack	10 (9.9%)	9 (11.5%)	1 (4.3%)	0.45
Pacemaker	11 (11.1%)	10 (13.2%)	1 (4.3%)	0.45
Logistic Euroscore I, median (IQR) [%]	14.0 (10.0–22.5)	17.0 (10.0–23.0)	11.0 (8.0–14.5)	0.08
STS, median (IQR) [%]	12.0 (5.0–24.0)	9.0 (5.0–20.0)	21.0 (8.5–30.0)	0.13
TG max, median (IQR) [mm Hg]	87.0 (71.5–108.0)	87.0 (70.5–106.5)	79.5 (62.0–90.0)	0.19
TG mean, median (IQR) [mm Hg]	51.0 (42.5–66.5)	52.0 (43.0–65.0)	48.5 (38.0–52.0)	0.26
AVA, median (IQR) [cm^2]	0.6 (0.4–0.8)	0.7 (0.6–0.8)	0.8 (0.6–1.0)	0.20
LVEF, median (IQR) [%]	60.0 (47.5–65.0)	60.0 (47.0–65.0)	62.0 (48.0–65.0)	0.51
Aortic regurgitation:				0.11
0	35 (34.7%)	24 (30.8%)	11 (47.8%)	
1	51 (50.5%)	44 (56.4%)	7 (30.4%)	
2	14 (13.9%)	9 (11.5%)	5 (21.7%)	
3	1 (1.0%)	1 (1.3%)	0 (0.0%)	

AVA — aortic valve area; CABG — coronary artery bypass graft; COPD — chronic obstructive pulmonary disease; eGFR — estimated glomerular filtration rate; IQR — interquartile range; LVEF — left ventricular ejection fraction; MI — myocardial infarction; NYHA — New York Heart Association; PCI — percutaneous coronary intervention; STS — The Society of Thoracic Surgeons; TG — transvalvular gradient

deployment, after PD, and at the end of TAVI procedure were present in 16 (19.8%), 16 (19.8%), and two (2.5%) patients in the balloon expandable valves group vs. eight (40.0%), seven (35.0%), and four (20.0%) patients in the self-expanding valves group (p = 0.08; p = 0.23; p = 0013), respectively.

DISCUSSION

Many factors may contribute significantly to clinical outcomes after TAVI. For instance, the presence of coronary artery disease and the occurence periprocedural ischaemic complications may worsen clinical outcomes [21, 22]. Another potential factor is the presence of PVL after TAVI. Importantly, PVL remains the factor linked directly to the procedure itself. Moderate-to-severe PVL had been previously identified as an independent predictor of death between 30 days and one year after TAVI with Medtronic CoreValve [23]. An impact of PVL on medium-term prognosis has recently been demonstrated also for the Edwards SAPIEN prosthesis [7]. Meta-analyses of multiple studies in the high-risk populations showed that moderate or severe PVL is an important determinant of mortality regardless of the implanted

Table 2. Procedural and follow-up data

	All patients (n = 101)	Post-dilatation (–) (n = 78)	Post-dilatation (+) (n = 23)	p
Transfemoral access	78 (77.2%)	57 (73.1%)	21 (91.3%)	< 0.001
Transapical access	21 (20.8%)	21 (26.9%)	0 (0.0%)	
Transaortic access	2 (2.0%)	0 (0.0%)	2 (8.7%)	
Medtronic CoreValve	20 (19.8%)	13 (16.7%)	7 (30.4%)	0.22
Edwards SAPIEN	77 (76.2%)	61 (78.2%)	16 (69.6%)	
Jena Valve	4 (4.0%)	4 (5.1%)	0 (0.0%)	
Prosthesis size:				0.86
23 mm	16 (15.8%)	14 (17.9%)	2 (8.7%)	
25 mm	2 (2.0%)	2 (2.6%)	0 (0.0%)	
26 mm	48 (47.5%)	36 (46.2%)	12 (52.2%)	
27 mm	1 (1.0%)	1 (1.3%)	0 (0.0%)	
29 mm	29 (28.7%)	21 (26.9%)	8 (34.8%)	
31 mm	5 (5.0%)	4 (5.1%)	1 (4.3%)	
Prosthesis size, median (IQR) [mm]	26.0 (26.0–29.0)	26.0 (26.0–29.0)	26.0 (26.0–29.0)	0.35
Annulus size, median (IQR) [mm]	23.0 (22.0–25.0)	23.0 (21.8–25.0)	23.0 (22.0–24.8)	0.50
Cover index, median (IQR) [%]	11.5 (8.7–15.4)	11.5 (8.7–15.3)	13.5 (10.3–15.4)	0.33
Ellipticity index, median (IQR) [%]	1.2 (1.0–1.2)	1.2 (1.0–1.2)	1.2 (1.0–1.3)	0.77
AR index before, median (IQR) [%]	28.4 (25.0–29.9)	29.4 (27.9–30.5)	23.4 (22.4–24.0)	< 0.001
AR index before < 25%	25 (24.8%)	4 (5.1%)	21 (91.3%)	< 0.001
AR index after, median (IQR) [%]	27.1 (26.1–28.3)	–	27.1 (26.1–28.3)	–
AR index after < 25%	1 (0.9%)	–	1 (4.3%)	–
Radiation dose, median (IQR) [mGy]	733.0 (634.0–831.5)	783.0 (678.0–841.0)	631.0 (606.0–739.5)	< 0.001
Contrast medium load, median (IQR) [mL]	100.0 (75.0–150.0)	100.0 (100.0–150.0)	75.0 (75.0–75.0)	< 0.001
Fluoroscopy time, median (IQR) [min]	14.0 (13.0–15.5)	14.0 (13.0–16.0)	13.0 (12.0–14.0)	0.013
TG max after TAVI, median (IQR) [mm Hg]	14.5 (10.8–19.0)	14.0 (10.6–19.0)	14.0 (10.0–19.0)	0.93
TG mean after TAVI, median (IQR) [mm Hg]	8.0 (6.0–10.0)	8.0 (6.0–9.6)	7.5 (6.0–11.0)	0.75
LVEF after, median (IQR) [%]	49.0 (42.8–60.0)	50.0 (44.0–60.0)	47.0 (38.5–49.5)	0.09

AR — aortic regurgitation; IQR — interquartile range; LVEF — left ventricular ejection fraction; TAVI — transcatheter aortic valve implantation; TG — transvalvular gradient

valve type [24, 25]. The occurrence of PVL after TAVI might be more frequent after direct valve implantation without balloon PD, resulting in more frequent PD afterwards [12].

We confirmed that balloon PD can effectively and safely reduce the degree of PVL after TAVI when the primary result of the implantation of the prosthesis is not optimal. PD has been performed due to frame under-expansion in most cases, and it was required in 22.7% of patients. This rate was quite similar to that reported in previous studies with a post-dilation rate of 30% to 38% after implantation of self-expanding prostheses and 28% to 41% for balloon-expandable valves [15, 17, 23, 24, 26]. PD might be associated with a higher rate of cardiovascular complications, conduction disturbances, annulus rupture, coronary obstruction, and cerebral embolism leading to stroke [1, 4]. These findings were not confirmed in our study because no differences in cardiovascular complications such as coronary obstruction, stroke, and death were observed. Interestingly, a trend towards improved mortality in patients with PD was noted. However, worse short- and long-term outcomes in patients without PD are possibly related to higher rates of blood transfusion and overall higher risk profile (logistic Euroscore I, NYHA class).

Post-implantation PVL is routinely assessed by control aortography and quantified according to VARC-2 criteria [20]. Echocardiography is helpful to identify the mechanism of PVL such as suboptimal frame expansion due to severe calcification in the native valve. The accurate assessment of PVL is an important means for determining the effectiveness of procedure. To quantify PVL grade more accurately, besides angiography and echocardiography, we used the previously validated ARI, for which a cut-off value of 25 has been shown to be an independent predictor of one-year mortality after

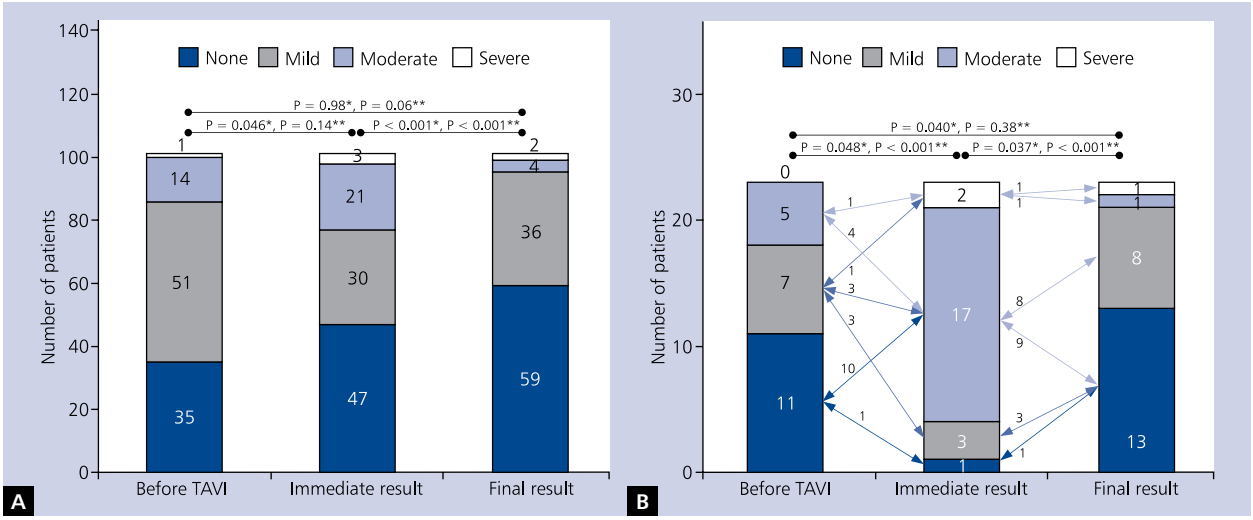

Figure 1. Severity of paravalvular leak (PVL) before and immediately after prosthesis deployment and at the end of the transcatheter aortic valve implantation (TAVI) procedure; **A.** For all patients; **B.** For patients requiring balloon post-dilatation); *p-value from χ^2 test; **p-value from McNemar's test for changes in the proportions of patients with "none/mild" vs. "moderate/severe" PVL

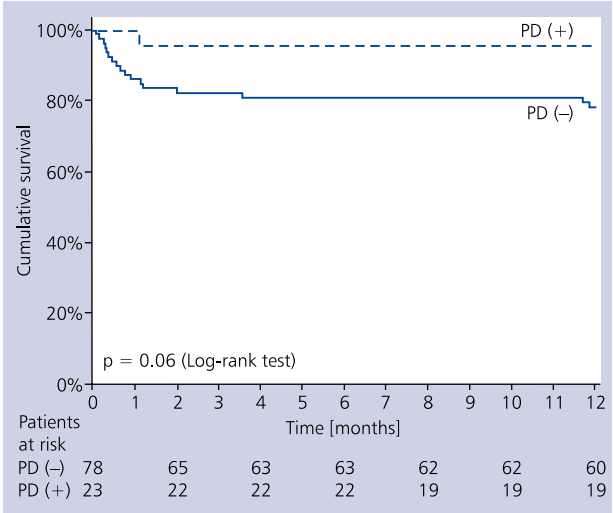

Figure 2. Kaplan–Meier curves for survival for patients stratified by the need for balloon post-dilatation (PD)

TAVI [9]. The ARI is a useful parameter to identify the need of PD but also to quantify the success of PD (additionally to imaging modalities) [9, 15]. Moreover, recently Sinning et al. [27] have shown that ARI integrating pre- and post-procedural haemodynamic status increases the discriminatory value of post-procedural ARI and is useful to identify patients with unfavourable prognosis. The difference in radiation dose, fluoroscopy time, and contrast load between patients with and without PD may be caused by some differences in baseline characteristics and more frequent use of the transapical approach in the PD (+) group.

Limitations of the study

The present investigation represents a single-centre experience with a relatively small sample size, which could be regarded as a limitation of the study. Because the study was not randomised we can expect some important differences in baseline characteristics between the two groups, which may influence mortality as well as other clinical outcomes. The limited sample size did not allow us to use a propensity matching technique to control for selection bias. Thus, the results, especially in terms of clinical outcomes, should be considered exploratory and hypothesis generating. The ARI might be confounded by high systemic blood pressure, diastolic dysfunction, myocardial ischaemia during and after valve deployment or PD, as well as the use of vasopressors during TAVI, and other causes that may lead to an increase of LV end-diastolic pressure leading to false positive ARI. Likewise, the heart rate and its undeniable influence on the diastolic aortic blood pressure affects the ARI. In spite of several limitations, our study represents the complete analysis of consecutive patients without any exclusion criteria and with follow-up data available for all patients.

CONCLUSIONS

Balloon post-dilatation may be safe and effective technique to reduce moderate to severe PVL after TAVI.

Conflict of interest: *none declared*

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OŚWIADCZENIE

Jako współautor pracy pt. „ Acute and Long-Term Outcomes of Percutaneous Balloon Aortic Valvuloplasty for the Treatment of Severe Aortic Stenosis" Catheter Cardiovasc Interv. 2017 Aug 1;90:303-310 oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji to: Analiza i interpretacja wyników oraz akceptacja ostatecznego tekstu publikacji.

Jednocześnie wyrażam zgodę na przedłożenie w/w pracy przez lek. Marzenę Daniec jako część rozprawy doktorskiej w formie spójnego tematycznie zbioru artykułów opublikowanych w czasopismach naukowych.

Oświadczam, iż samodzielna i możliwa do wyodrębnienia część ww. pracy wykazuje indywidualny wkład lek. Marzeny Daniec przy opracowywaniu koncepcji, wykonywaniu części eksperymentalnej, opracowaniu i interpretacji wyników tej pracy.

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(podpis współautora)

Kraków, dnia 07.2017

Prof. dr hab. n. med. Dariusz Dudek
specjalista chorób wewnętrznych; specjalista kardiolog
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(tytuł zawodowy, imię i nazwisko)

OŚWIADCZENIE

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(podpis współautora)

Kraków, dnia 06.03.2018

Dr hab. n. med. Artur Dziewierz
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OŚWIADCZENIE

Jako współautor pracy pt. „In-hospital and long-term outcomes of percutaneous balloon aortic valvuloplasty with concomitant percutaneous coronary intervention in patients with severe aortic stenosis" J Interv Cardiol. 2018 Feb;31:60-67 oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji to: Analiza i interpretacja wyników, współudział w przygotowaniu tekstu publikacji oraz akceptacja ostatecznego tekstu publikacji.

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.....
(podpis współautora)

Kraków, dnia 18.03.2018

Dr hab. n. med. Paweł Kleczyński
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(tytuł zawodowy, imię i nazwisko)

OŚWIADCZENIE

Jako główny/korespondencyjny autor pracy pt. „Impact of post-dilatation on the reduction of paravalvular leak and mortality after transcatheter aortic valve implantation" Kardiol Pol. 2017;75:742-748 oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji to: analiza i interpretacja wyników, współudział w przygotowaniu tekstu publikacji, współudział w opracowaniu koncepcji badania/rejestru oraz akceptacja ostatecznego tekstu publikacji.

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Kraków, dnia 6.5.2018

Dr n. med. Jarosław Trębacz
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OŚWIADCZENIE

Jako współautor pracy pt. „Impact of post-dilatation on the reduction of paravalvular leak and mortality after transcatheter aortic valve implantation" Kardiol Pol. 2017;75:742-748 oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji to: Analiza i interpretacja wyników oraz akceptacja ostatecznego tekstu publikacji.

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.....
(podpis współautora)

Kraków, dnia 05/03/2018

Lek. med. Maciej Bagieński
specjalista kardiolog
.....
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Jako współautor pracy pt. „Impact of post-dilatation on the reduction of paravalvular leak and mortality after transcatheter aortic valve implantation" Kardiol Pol. 2017;75:742-748 oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji to: Analiza i interpretacja wyników oraz akceptacja ostatecznego tekstu publikacji.

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Maciej Bagieński
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Kraków, dnia 19.03.2018

Dr n. med. Łukasz Rzeszutko
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.....
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Kraków, dnia. 10.04.2018

Dr n. med. Danuta Sorysz
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OŚWIADCZENIE

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Kraków, dnia 9.03.2018

Prof. dr hab. n. med. Dariusz Dudek
specjalista chorób wewnętrznych; specjalista kardiolog
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(tytuł zawodowy, imię i nazwisko)

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Dem Dud
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(podpis współautora)

Kraków, dnia 06.03.2018

Dr hab. n. med. Artur Dziewierz
specjalista chorób wewnętrznych; specjalista kardiolog
.....
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OŚWIADCZENIE

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.....

(podpis współautora)

Kraków, dnia 18.05.2018

Dr hab. n. med. Paweł Kleczyński
specjalista chorób wewnętrznych; specjalista kardiolog
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(tytuł zawodowy, imię i nazwisko)

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.....
(podpis współautora)

Kraków, dnia 05.03.2018

Lek. Agata Krawczyk-Ożóg

.....

(tytuł zawodowy, imię i nazwisko)

OŚWIADCZENIE

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Agata Krawczyk-Ożóg

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Kraków, dnia 19.03.2018

Dr n. med. Łukasz Rzeszutko
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.....
(podpis współautora)

Kraków, dnia 10.03.2018

Dr n. med. Danuta Sorysz
specjalista chorób wewnętrznych; specjalista kardiolog
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(tytuł zawodowy, imię i nazwisko)

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Kraków, dnia 8.03.2018

Prof. dr hab. n. med. Dariusz Dudek
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OŚWIADCZENIE

Jako współautor pracy pt. „In-hospital and long-term outcomes of percutaneous balloon aortic valvuloplasty with concomitant percutaneous coronary intervention in patients with severe aortic stenosis" J Interv Cardiol. 2018 Feb;31:60-67 oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji to: Analiza i interpretacja wyników oraz współudział w opracowaniu koncepcji badania/rejestru.

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(podpis współautora)