Peer review file

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Reviewer A

Comment #1: The authors provide an overview on the impact of the COVID-19 pandemic on referrals for AVR in patients with symptomatic severe aortic stenosis in a single center compared to 2018 and 2019. The study is limited by the overall low number of cases reported and the lack of a "fancy" take home message.

Reply #1:
We do agree completely with the Reviewer regarding the above-mentioned limitation. In the last passage of 'Discussion' section, an issue of small number of cases was also stressed. Additionally, owing to additional analysis of early results conclusions were rewritten and we hope they include expected take home message.

Changes in the text #1:
The following sentences have been added (regarding low number of cases):
First, the number of patients who underwent invasive treatment for severe AS was relatively low and this fact could have impacted the results of the statistical analysis. However, even in this group significant changes were noted. One can not exclude that involving more patients might have been disclosed additional differences between examined periods, for example early mortality.

The following sentences have been added to the section 'Conclusions' (in a response to 'a lack of take home message' pointed by the Reviewer):
This shift into less invasive method of treatment of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes. This strategy fulfilled expectations of health care system during SARS-CoV-2 pandemic.
Consequently, a shortcut of this conclusion was also added to the appropriate part of abstract. 'The shift into less invasive treatment method of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes.'

Comment #2: The reviewer believes that the manuscript would gain impact if the authors would focus first on the characteristics of patients undergoing AVR (TAVR+SAVR) in 2020 versus 2018/19 rather than separating the groups in TAVR and SAVR considering the low number of cases (maybe authors should consider including other centers).

Reply #2: Before we started writing our manuscript we had analyzed all patients with aortic stenosis (AS) together. However, due to a commonly known fact that TAVI patients are much different than SAVR ones, we did not dare to confine our analysis just to all AS patients before and during pandemic as it could have resulted in a large bias as a consequence of patients' heterogeneity (additionally having in mind a relatively small number of cases). Moreover, we showed in our study that COVID-19 pandemic changed only clinical profile of SAVR cases but not TAVI. Therefore, at the time of manuscript preparation we did skip the aforementioned idea of analysis as one SA group. However, being encouraged by the Reviewer, the majority of data such as preoperative characteristics and echocardiographic findings as well as variables characterizing postoperative course (intubation and in-hospital stay times), were also presented and compared between two groups (COV(-) vs. COV(+), ie. before (years 2018 through 2019) and after (year 2020) SARS-CoV-2 pandemic outbreak. As a consequence, we had to revise our manuscript and add some sentences in an 'Abstract' and 'Results' sections. Moreover, we compressed preoperative data of TAVI and SAVR patients to present them in one table (Table I). In this table, the first two columns present data for a whole groups COV(-) vs COV(+).
We agree that it is a very good idea to invite other centers and to analyze bigger group of cases. Owing your remark, our team has already decided to gather 4-5 cardiac surgical centers to increase substantially number of participants. However, the results will be presented in the future.

Changes in the text #2:
In the 'Abstract' the following sentence was added:
[…] During the pandemic, a change in applied therapeutic methods and differences in

patients' clinical profile did not have an unfavorable impact on in-hospital mortality (2.0% before vs. 3.6% during pandemic) and morbidity. Of note, intubation time and in-hospital stay were significantly shorter ($p<0.05$) in 2020 (4.2 hours and 7.5 days) than in the previous years (7.5 hours and 9.0 days, respectively).

In the 'Results' section the following sentences were added:

3.2. Preoperative patients' characteristics

[…] Therefore, they were entered into the further analysis as a one group (COV(-)).

3.5. Postoperative course

Overall, short-term mortality defined as all deaths that occurred with the first 30 days following procedure irrespective of patient stay (hospital, rehabilitation center, home) was 2.5% (n=4), two fatal cases in both groups. Three of them represented COV(-) (mortality rate 2.9%) while one COV(+) group (1.8%).

[…] Comparison of intubation time and in-hospital stay revealed the their median times of all patients irrespective of valve implantation technique was significantly shorter in the year of SARS-CoV-2 pandemic than previously (see Figure 2). It probably resulted from higher contribution of TAVI procedures after pandemic outbreak.

We compressed preoperative data of TAVI and SAVR patients to present them in one table (Table I). In this table, the first two columns present data for a whole groups COV(-) vs COV(+). As there was no place for p values presentations, we indicated differences of statistical significance with symbol '#'.

Additionally, a new Figure 2 replaced the previous one. The current one presents some early results and comparison between 2020 vs 2018/19 (both suggested by two Reviewers). Consequently, a caption of Figure 2 had to be changed.

Figure 2. Comparison of intubation time and in-hospital stay length

both continuous variables are expressed as the medians since they have not fulfilled criteria of normal distribution; & it refers to all cases, including those who were not intubated during procedures.

Abbreviations: COV (+)/(-) = patients who were operated on during (+) or before (-) SARS-CoV-2 pandemic outbreak.

Comment #3:

The most important finding relates to the fact that during 2020 patients undergoing AVR had an overall higher risk according to ES II due to the restrictions implemented by healthcare authorities. It would have been interesting to understand whether this shift towards a higher risk populations also affected short/mid term outcomes (complications, mortality, length of hospitalization, etc) for AVR in general and then in a second step for both procedures.

Reply #3:

Although, the primary purpose of our paper was just presentation of clinical profile and characteristic of treated individuals with severe aortic stenosis, Your and another Reviewer suggestion encouraged us to analyze also the early outcomes having in mind an overall higher risk of patients, especially in SAVR group. The findings of short outcomes analysis include not only mortality and morbidity but also supported ventilation time and length of hospitalization. They have been added to the revised version of our manuscript.

Inclusion of short outcomes analysis resulted in the changes in 'Introduction', 'Material and methods', 'Results' (two tables called respectively Table 4 and Table 5 were added and the Figure 2 was also replaced; the current one presents graphically a comparison of some postoperative data), 'Discussion' as well as 'Conclusions' sections.

Changes in the text #3:

'Abstract'

[…] We assessed if there were any differences regarding patients' clinical profile, applied therapeutic method, procedure complexity and early clinical outcomes.

[…] During the pandemic, a change in applied therapeutic methods and differences in patients' clinical profile did not have an unfavorable impact on in-hospital mortality (2.0% before vs. 3.6% during pandemic) and morbidity. Of note, intubation time and in-hospital stay were significantly shorter ($p<0.05$) in 2020 (4.2 hours and 7.5 days) than in the previous years (7.5 hours and 9.0 days, respectively).

[…] The shift into less invasive treatment method of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes.

‘Introduction’

Therefore, the purpose of our cross-sectional study was to determine if the COVID-19 pandemic had any impact on management, the clinical profile and early outcomes of patients treated for severe AS.

‘Material and methods’

A subsection entitled ‘2.5. Postoperative period’ has been added

2.5. Postoperative period

The selected individuals after TAVI (with intraprocedural complications or these considered preoperatively as very high risk) and all patients who got SAVR were transferred to the postoperative ICU, intubated and mechanically ventilated. According to the hospital rules, patients in stable clinical status after ICU stay were further treated at either the cardiac surgery (SAVR) or cardiology (TAVI) ward. The subjects after open surgical operations were usually discharged to rehabilitation centers whereas those following percutaneous interventions usually were sent home directly.

Consequently, the numbering of the subsequent subsections of ‘Material and methods’ have also been changed (2.5 to 2.6 and 2.6 to 2.7, respectively).

In subsection ‘2.6. Parameters included’ the following text was added:

[…] Postoperative in-hospital course, including mortality and morbidity was also analyzed. Moreover, a length of endotracheal intubation (if applicable), ICU and in-hospital stays were evaluated. Additionally, the following serious adverse events were taken into account:

-myocardial infarction (defined if all conditions such as significant increase in troponin I concentration, ischemic changes in electrocardiogram and new local disturbances in myocardial contractility were fulfilled simultaneously),

-atrio-ventricular block (AVB) requiring permanent pacemaker implantation,

-renal failure treated by means of renal replacement therapy (continuous veno-venous hemodialysis, CVVHD),

-respiratory failure if patients had to be intubated longer than 12 hours or be reintubated,

-stroke (confirmed in neurological (specialist consultation) and imaging examinations (computed tomography or magnetic resonance imaging)),

-bleeding from surgical access (TAVI) or bleeding/tamponade requiring chest re-

exploration,

-deep surgical site infection (DSSI) treated with repeat sternal reosteosynthesis (after SAVR),

-peripheral TAVI access serious complications (eg., artery dissection, false aneurysm) if vascular open or intravascular interventions were necessary.

'Results'

3.5. Postoperative course

Overall, short-term mortality defined as all deaths that occurred within the first 30 days following procedure irrespective of patient stay (hospital, rehabilitation center, home) was 2.5% (n=4), two fatal cases in both subgroups. Mortality rate among COV(-) individuals was 2.0% while 3.6% in COV(+) group (ns). Taking into account a method of aortic valve implantation, single SAVR patients died either in the years 2018-2019 or in 2020 (both had combined procedures, SAVR completed by CABG) whereas all TAVI subjects (n=2) before SARS-CoV-2 pandemic. The reasons of death myocardial ischemia – induced low cardiac output syndrome (LCOS) (n=2; on 3rd and 5th postoperative days) in SAVR group whereas fatal bleeding due to perforation of left ventricle (intraoperative death) and LCOS preceding multi-organ failure (MOF) in TAVI subjects.

The other postprocedural serious adverse events are summarized in Table 4. Of note, the rate of them was comparable in the consecutive years in TAVI group (28% in 2018, 36% in 2019 and 24% in 2020; ns) while in SAVR subset it was significant higher (p=0.048) in 2020 (42%) than in the years 2018-2019 (19%).

Additionally, comparison of intubation time and in-hospital stay revealed their median times for of all patients irrespective of valve implantation technique was significantly shorter in the year of SARS-CoV-2 pandemic than previously (see Figure 2). It probably resulted from higher contribution of TAVI procedures after pandemic outbreak. Detailed analysis of the aforementioned variables of the postoperative course were comparable within both subgroups in the consecutive years (SAVR 2018 = SAVR 2019 = SAVR 2020; TAVI 2018 = TAVI 2019 = TAVI 2020) but notable they were always markedly shorter in TAVI individuals (ie. TAVI 2018<SAVR 2018, TAVI 2019<SAVR 2019, TAVI 2020<SAVR 2020) (see Table 5). As it is stated in the text two additional table 4 and 5 completed presentation of postoperative course analysis.

‘Figures’

Figure 2 was also replaced and the current one refers to early clinical results.

‘Discussion’

Two below paragraphs have been added to ‘Discussion’ section:

Herein, we also observed the changed management with AS patients in the pandemic era did not negatively impact the early clinical outcomes expressed as in-hospital mortality and prevalence of serious adverse events. In our group, overall mortality rate was comparable or slightly higher than in the previously published studies [37, 38]. Contrary to them, in our group of SAVR cases, even one thirds had to undergo simultaneous CABG [17, 18]. The latter one was proved to have unfavorable influence on both early and late outcomes, particularly in women [39-41]. Moreover, CAD accompanying hypertrophic LV myocardium induced by severe aortic valve stenosis poses a high risk of intraoperative myocardial ischemia. Of note, in both patients who died soon after surgery, preoperative coronary angiography revealed significant lesions that had to be addressed during surgery.

Very important issue during the SARS-CoV-2 pandemic is a limited number of beds with monitoring of vital signs. Therefore, currently all actions resulting in the shortening of in-hospital stay are welcome. We did observe the shortest hospitalization time in 2020, mainly due to an increased rate of TAVI procedures. The latter ones, especially these performed on moderate risk patients and with uneventful postprocedural course, were found to be associated with earlier discharge than after SAVR. Our findings regarding this issue supported the previous reports [17, 18, 42, 43]. Some of them stressed economic aspects of AS treatment [44]. It was showed that more common application of TAVI procedures, in spite of high price of implanted bioprostheses, had important implications in the era of constrained resources with a growing emphasis on reducing health care costs [44].

‘Conclusions’

This shift into less invasive method of treatment of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes. This strategy fulfilled expectations of health care system during SARS-CoV-2 pandemic.

Comment #4:

- Figure 2 is redundant as ESII score are reported in the table

Reply #4:

We agree completely. Therefore, the Figure 2 has been replaced.

Changes in the text #4:

Not only Figure 2 was replaced but also the Figure 2 caption had to be corrected:

Figure 2. Comparison of intubation time and in-hospital stay length

both continuous variables are expressed as the medians since they have not fulfilled criteria of normal distribution; & it refers to all cases, including those who were not intubated during procedures.

Abbreviations: COV (+)/(-) = patients who were operated on during (+) or before (-) SARS-CoV-2 pandemic outbreak.

Comment #5:

-tables describing the characteristics of SAVR and TAVR patients should include similar variables

Reply #5:

We did corrected/completed variables describing the characteristics of SAVR and TAVI patients and in the revised version of our manuscript they include the same variables. Additionally, to follow the earlier recommendation, we put all preoperative data in one table, numbered as ‘1’ in the revised version of our manuscript.

Changes in the text #5:

Table 1 has been reorganized and in the current form includes preoperative data of all cases, TAVI as well as SAVR patients.

Comment #6:

manuscript should be double checked by a native speaker and corrected for spelling mistakes

Reply #6: According to Reviewer remark, this manuscript had been checked by a native speaker and corrected for spelling mistakes.

Changes in the text #6:
All changes suggested by a native speaker are in blue.

Minor remarks:
Comments #7:
- line 91: please remove "developed countries"....
- line 155: "once the prosthetic..... "please correct the sentence
-line 195: "to compared..." please correct the sentence
- line 250: "due to lack....." please correct the sentence

Reply #7:
Thank you very much for your remarks. All the aforementioned mistakes have been corrected and ‘developed countries’ removed.

Changes in the text #7:
Line 91: ‘developed countries’ has been deleted.
Lines 158-160 (in the previous version line 155) […] Once the prosthesis was correctly positioned and expanded, the contrast medium was injected to check for the presence of paravalvular leak. […]
Lines 222-224 (in the previous version line 195) […] To compare COV (-) with COV (+) subjects, unpaired T-test, Mann-Witney U and $\chi 2$ test with or without Yates correction were employed. […]
Lines 313-315 (in the previous version line 250) […] Due to a lack of long-term data on the rate of bioprosthetic structural valve deterioration in younger individuals, low risk but middle-aged patients should still undergo SAVR [16, 20].

Comment #8:
- Ref 16. please cite the original reference of the most updated ESC/EATCS

Reply #8:

Ref. 16 has been changed to the most updated ESC/EACTS guidelines.

Changes in the text #8:
The Ref. 16 in the corrected version of manuscript is:
[16] H. Baumgartner, V. Falk, J.J. Bax, et al., 2017 ESC/EACTS Guidelines for the management of valvular heart disease, Eur. Heart J. 36 (38) (2017) 2739–2791. https://doi.org/10.1093/eurheartj/ehx391.

Comment #9:
Guidelines
- please cite recent randomized trials in low-risk patients (PARTNER 3, EVOLUT) while discussing this topic in the discussion section.

Reply #9:
Recent randomized trials in low-risk patients (PARTNER 3, EVOLUT) has been cited at least 3 times.

Changes in the text #9:
[17] M.J. Mack, M.B. Leon, V.H. Thourani, et al., on behalf of the PARTNER 3 Investigators, Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients, N. Engl. J. Med. 380 (2019) 1695-1705. https://doi.org/10.1056/NEJMoa1814052
[18] J.J. Popma, G.M. Deeb, S.J. Yakubov, et al., for the Evolut Low Risk Trial Investigators, Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N. Engl. J. Med. 380 (2019) 1706-1715. https://doi.org/10.1056/NEJMoa1816885.
Consequently, a few following sentences have been added to the ‘Discussion’ section […] Moreover, the recent trials that involved low risk AS subjects, such as PARTNER 3 or EVOLUT, showed better outcomes, including both mortality and morbidity, following TAVI than after SAVR [17, 18]. The significance of these findings is of crucial importance as most patients (even up to 80%) with severe AS are usually at low surgical risk [19]. We must be aware that they referred not to all AS subjects but only to those who were appropriate candidates for implantation of

biological prostheses. […]
… and numbering of the following references had to be changed.

Reviewer B

The authors investigated the changes in the treatment strategy of AS by emerged COVID-19 and have found that the number of patients who underwent TAVI increased compared with SVR while operative risk has become higher in SVR patients. It is a single center experience and statistical analyses have been done.

Comment #1:
After I have read through this paper, I am unable to find the message and clinical implication of this report as an original article because decision of treatment strategy of either SVR or TAVI had been done in this institute probably in the heart team, and the changes in treatment strategy has been analyzed in the same institute. Instead of original article, I think that these results are rather like annual report.

Reply #1:
We hope that inclusion of detailed analysis of short-term outcomes, make our article more original than just annual report. It is true that decision regarding therapeutic method of AS patients had been done by the heart team but pandemic and epidemiological environment had impact on its decision in the last months. However, to improve value and scientific quality of our paper, detailed analysis of the short-term postprocedural outcomes have been added. In a consequence, the appropriate corrections in almost all sections of our manuscript had to be done.

Changes in the text #2:
All corrections related to the inclusion of short-term outcomes are listed below:
‘Abstract’
[…] We assessed if there were any differences regarding patients' clinical profile, applied therapeutic method, procedure complexity and early clinical outcomes.
[…] During the pandemic, a change in applied therapeutic methods and differences in patients’ clinical profile did not have an unfavorable impact on in-hospital mortality

(2.0% before vs. 3.6% during pandemic) and morbidity. Of note, intubation time and in-hospital stay were significantly shorter ($p<0.05$) in 2020 (4.2 hours and 7.5 days) than in the previous years (7.5 hours and 9.0 days, respectively).
[…] The shift into less invasive treatment method of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes.

‘Introduction’

Therefore, the purpose of our cross-sectional study was to determine if the COVID-19 pandemic had any impact on management, the clinical profile and early outcomes of patients treated for severe AS.

‘Material and methods’

A subsection entitled ‘2.5. Postoperative period’ has been added

2.5. Postoperative period

The selected individuals after TAVI (with intraprocedural complications or these considered preoperatively as very high risk) and all patients who got SAVR were transferred to the postoperative ICU, intubated and mechanically ventilated. According to the hospital rules, patients in stable clinical status after ICU stay were further treated at either the cardiac surgery (SAVR) or cardiology (TAVI) ward. The subjects after open surgical operations were usually discharged to rehabilitation centers whereas those following percutaneous interventions usually were sent home directly.

Consequently, the numbering of the subsequent subsections of ‘Material and methods’ have also been changed (2.5 to 2.6 and 2.6 to 2.7, respectively).

In subsection ‘2.6. Parameters included’ the following text was added:

[…] Postoperative in-hospital course, including mortality and morbidity was also analyzed. Moreover, a length of endotracheal intubation (if applicable), ICU and in-hospital stays were evaluated. Additionally, the following serious adverse events were taken into account:

-myocardial infarction (defined if all conditions such as significant increase in troponin I concentration, ischemic changes in electrocardiogram and new local disturbances in myocardial contractility were fulfilled simultaneously),

-atrio-ventricular block (AVB) requiring permanent pacemaker implantation,

-renal failure treated by means of renal replacement therapy (continuous veno-venous hemodialysis, CVVHD),

-respiratory failure if patients had to be intubated longer than 12 hours or be reintubated,
-stroke (confirmed in neurological (specialist consultation) and imaging examinations (computed tomography or magnetic resonance imaging)),
-bleeding from surgical access (TAVI) or bleeding/tamponade requiring chest re-exploration,
-deep surgical site infection (DSSI) treated with repeat sternal reosteosynthesis (after SAVR),
-peripheral TAVI access serious complications (eg., artery dissection, false aneurysm) if vascular open or intravascular interventions were necessary.

‘Results’

3.5. Postoperative course

Overall, short-term mortality defined as all deaths that occurred within the first 30 days following procedure irrespective of patient stay (hospital, rehabilitation center, home) was 2.5% (n=4), two fatal cases in both subgroups. Mortality rate among COV(-) individuals was 2.0% while 3.6% in COV(+) group (ns). Taking into account a method of aortic valve implantation, single SAVR patients died either in the years 2018-2019 or in 2020 (both had combined procedures, SAVR completed by CABG) whereas all TAVI subjects (n=2) before SARS-CoV-2 pandemic. The reasons of death myocardial ischemia – induced low cardiac output syndrome (LCOS) (n=2; on 3rd and 5th postoperative days) in SAVR group whereas fatal bleeding due to perforation of left ventricle (intraoperative death) and LCOS preceding multi-organ failure (MOF) in TAVI subjects.

The other postprocedural serious adverse events are summarized in Table 4. Of note, the rate of them was comparable in the consecutive years in TAVI group (28% in 2018, 36% in 2019 and 24% in 2020; ns) while in SAVR subset it was significant higher (p=0.048) in 2020 (42%) than in the years 2018-2019 (19%).

Additionally, comparison of intubation time and in-hospital stay revealed their median times for of all patients irrespective of valve implantation technique was significantly shorter in the year of SARS-CoV-2 pandemic than previously (see Figure 2). It probably resulted from higher contribution of TAVI procedures after pandemic outbreak. Detailed analysis of the aforementioned variables of the postoperative course were comparable within both subgroups in the consecutive years

(SAVR 2018 = SAVR 2019 = SAVR 2020; TAVI 2018 = TAVI 2019 = TAVI 2020) but notable they were always markedly shorter in TAVI individuals (ie. TAVI 2018<SAVR 2018, TAVI 2019<SAVR 2019, TAVI 2020<SAVR 2020) (see Table 5). As it is stated in the text two additional table 4 and 5 completed presentation of postoperative course analysis.

'Figures'

Figure 2 was also replaced and the current one refers to early clinical results.

'Discussion'

Two below paragraphs have been added to 'Discussion' section:

Herein, we also observed the changed management with AS patients in the pandemic era did not negatively impact the early clinical outcomes expressed as in-hospital mortality and prevalence of serious adverse events. In our group, overall mortality rate was comparable or slightly higher than in the previously published studies [37, 38]. Contrary to them, in our group of SAVR cases, even one thirds had to undergo simultaneous CABG [17, 18]. The latter one was proved to have unfavorable influence on both early and late outcomes, particularly in women [39-41]. Moreover, CAD accompanying hypertrophic LV myocardium induced by severe aortic valve stenosis poses a high risk of intraoperative myocardial ischemia. Of note, in both patients who died soon after surgery, preoperative coronary angiography revealed significant lesions that had to be addressed during surgery.

Very important issue during the SARS-CoV-2 pandemic is a limited number of beds with monitoring of vital signs. Therefore, currently all actions resulting in the shortening of in-hospital stay are welcome. We did observe the shortest hospitalization time in 2020, mainly due to an increased rate of TAVI procedures. The latter ones, especially these performed on moderate risk patients and with uneventful postprocedural course, were found to be associated with earlier discharge than after SAVR. Our findings regarding this issue supported the previous reports [17, 18, 42, 43]. Some of them stressed economic aspects of AS treatment [44]. It was showed that more common application of TAVI procedures, in spite of high price of implanted bioprostheses, had important implications in the era of constrained resources with a growing emphasis on reducing health care costs [44].

'Conclusions'

This shift into less invasive method of treatment of aortic stenosis patients

resulted in shortening of in-hospital stay without compromise of short-term outcomes. This strategy fulfilled expectations of health care system during SARS-CoV-2 pandemic.

Comment #2:
I think this topic needs to be analyzed and discussed in larger picture because role allotment of treating AS among hospitals in the country or district may be necessary to make strategies which are believed to be most suitable for each patients which is originally not affected by other factors; for example some hospitals are allotted for cardiac surgery and others for COVID-19. It is rather a social issue. Therefore, I wonder if any new finding or suggestion for improving the clinical practice is obtained from the results drawn from the study. Excuse me if it is my misconception.

Reply #2:
Absolutely, you are right with the aforementioned conception but I am afraid that not in the current stage of pandemic in Europe, also in Poland. At the beginning it was possible to allot some hospitals for cardiac surgery and others for COVID-19. To put it honestly, such strategy had been proposed by our government and it seemed to work but prior to outbreak of the second wave of SARS-CoV-2 pandemic. Unfortunately, currently we have COVID positive patients waiting for TAVI/SAVR procedures in all cardiac surgical centers.
Concluding, we think that our strategy to postpone elective and asymptomatic SAVR subjects (resulted in an increasing rate of high risk AS patients in 2020) and to perform as much as necessary TAVI procedures, saving ICU and hospital facilities, is right.

Changes in the text #2: N/A

Reviewer C

Comment #1:
The authors provide a photo of the activity related to treatment of severe aortic stenosis during the COVID-19 pandemic. The topic is not very interesting, and it does

not reach a satisfactory level of interest. The manuscript could be better match the characteristics of an editorial, than of an original article.

Reply#1:
We hope that inclusion of the detailed analysis of early outcomes following SAVR and TAVI procedures increased the scientific value of our paper. This action required substantial revision and changes in almost all sections of the manuscript.

Changes in the text#1:
All corrections related to the inclusion of short-term outcomes are listed below:
‘Abstract’
[…] We assessed if there were any differences regarding patients' clinical profile, applied therapeutic method, procedure complexity and early clinical outcomes.
[…] During the pandemic, a change in applied therapeutic methods and differences in patients’ clinical profile did not have an unfavorable impact on in-hospital mortality (2.0% before vs. 3.6% during pandemic) and morbidity. Of note, intubation time and in-hospital stay were significantly shorter ($p<0.05$) in 2020 (4.2 hours and 7.5 days) than in the previous years (7.5 hours and 9.0 days, respectively).
[…] The shift into less invasive treatment method of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes.
‘Introduction’
Therefore, the purpose of our cross-sectional study was to determine if the COVID-19 pandemic had any impact on management, the clinical profile and early outcomes of patients treated for severe AS.
‘Material and methods’
A subsection entitled ‘2.5. Postoperative period’ has been added
2.5. Postoperative period

The selected individuals after TAVI (with intraprocedural complications or these considered preoperatively as very high risk) and all patients who got SAVR were transferred to the postoperative ICU, intubated and mechanically ventilated. According to the hospital rules, patients in stable clinical status after ICU stay were further treated at either the cardiac surgery (SAVR) or cardiology (TAVI) ward. The subjects after open surgical operations were usually discharged to rehabilitation

centers whereas those following percutaneous interventions usually were sent home directly.

Consequently, the numbering of the subsequent subsections of 'Material and methods' have also been changed (2.5 to 2.6 and 2.6 to 2.7, respectively).

In subsection '2.6. Parameters included' the following text was added:

[…] Postoperative in-hospital course, including mortality and morbidity was also analyzed. Moreover, a length of endotracheal intubation (if applicable), ICU and in-hospital stays were evaluated. Additionally, the following serious adverse events were taken into account:

-myocardial infarction (defined if all conditions such as significant increase in troponin I concentration, ischemic changes in electrocardiogram and new local disturbances in myocardial contractility were fulfilled simultaneously),

-atrio-ventricular block (AVB) requiring permanent pacemaker implantation,

-renal failure treated by means of renal replacement therapy (continuous veno-venous hemodialysis, CVVHD),

-respiratory failure if patients had to be intubated longer than 12 hours or be reintubated,

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'Results'

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whereas all TAVI subjects (n=2) before SARS-CoV-2 pandemic. The reasons of death myocardial ischemia – induced low cardiac output syndrome (LCOS) (n=2; on 3rd and 5th postoperative days) in SAVR group whereas fatal bleeding due to perforation of left ventricle (intraoperative death) and LCOS preceding multi-organ failure (MOF) in TAVI subjects.

The other postprocedural serious adverse events are summarized in Table 4. Of note, the rate of them was comparable in the consecutive years in TAVI group (28% in 2018, 36% in 2019 and 24% in 2020; ns) while in SAVR subset it was significant higher (p=0.048) in 2020 (42%) than in the years 2018-2019 (19%).

Additionally, comparison of intubation time and in-hospital stay revealed their median times for of all patients irrespective of valve implantation technique was significantly shorter in the year of SARS-CoV-2 pandemic than previously (see Figure 2). It probably resulted from higher contribution of TAVI procedures after pandemic outbreak. Detailed analysis of the aforementioned variables of the postoperative course were comparable within both subgroups in the consecutive years (SAVR 2018 = SAVR 2019 = SAVR 2020; TAVI 2018 = TAVI 2019 = TAVI 2020) but notable they were always markedly shorter in TAVI individuals (ie. TAVI 2018<SAVR 2018, TAVI 2019<SAVR 2019, TAVI 2020<SAVR 2020) (see Table 5). As it is stated in the text two additional table 4 and 5 completed presentation of postoperative course analysis.

‘Figures’

Figure 2 was also replaced and the current one refers to early clinical results.

‘Discussion’

Two below paragraphs have been added to ‘Discussion’ section:

Herein, we also observed the changed management with AS patients in the pandemic era did not negatively impact the early clinical outcomes expressed as in-hospital mortality and prevalence of serious adverse events. In our group, overall mortality rate was comparable or slightly higher than in the previously published studies [37, 38]. Contrary to them, in our group of SAVR cases, even one thirds had to undergo simultaneous CABG [17, 18]. The latter one was proved to have unfavorable influence on both early and late outcomes, particularly in women [39-41]. Moreover, CAD accompanying hypertrophic LV myocardium induced by severe aortic valve stenosis poses a high risk of intraoperative myocardial ischemia. Of note,

in both patients who died soon after surgery, preoperative coronary angiography revealed significant lesions that had to be addressed during surgery.

Very important issue during the SARS-CoV-2 pandemic is a limited number of beds with monitoring of vital signs. Therefore, currently all actions resulting in the shortening of in-hospital stay are welcome. We did observe the shortest hospitalization time in 2020, mainly due to an increased rate of TAVI procedures. The latter ones, especially these performed on moderate risk patients and with uneventful postprocedural course, were found to be associated with earlier discharge than after SAVR. Our findings regarding this issue supported the previous reports [17, 18, 42, 43]. Some of them stressed economic aspects of AS treatment [44]. It was showed that more common application of TAVI procedures, in spite of high price of implanted bioprostheses, had important implications in the era of constrained resources with a growing emphasis on reducing health care costs [44].

‘Conclusions’

This shift into less invasive method of treatment of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes. This strategy fulfilled expectations of health care system during SARS-CoV-2 pandemic.

However, many point should be clarified:

Comment #2:

- line 249 up to 252: the two sentences are in contrast. In particular the guideline does not suggest yet TAVI for low risk patients;

Reply #2:

Of course, you are absolutely right with the guidelines.

Although recent trials such as PARTNER 3 or EVOLUT advocate not inferior or even better outcomes in low surgical risk patients, valid guidelines, issued in 2017 did not recommend TAVI for this group of AS patients.

Changes in the text #2:

The two sentences (lines 249 through 252 in the previous version) were changed and therefore clarified. In the revised version (lines 306 to 315) they are separated by

additional sentences.

[…] Consequently, according to the current ESC/EACTS guidelines, TAVI can be recommended not only in high but also moderate risk patients [16]. Moreover, the recent trials that involved low risk AS subjects, such as PARTNER 3 or EVOLUT, showed better outcomes, including both mortality and morbidity, following TAVI than after SAVR [17, 18]. The significance of these findings is of crucial importance as most patients (even up to 80%) with severe AS are usually at low surgical risk [19]. We must be aware that they referred not to all AS subjects but only to those who were appropriate candidates for implantation of biological prostheses. Due to a lack of long-term data on the rate of bioprosthetic structural valve deterioration in younger individuals, low risk but middle-aged patients should still undergo SAVR [16, 20].

Comment #3:

- the title states "single center": I did not find the name of the center;

Reply #3:

The name of the center was added in '2.1. Patients' subsection

Changes in the text #3:

Lines 128 to 129: […] All patients were treated invasively for severe AS in the Department of Cardiac Surgery and Transplantology in Poznan (Poland). […]

Comment #4:

- the authors disclosed "Provision of study materials or patients: BP, AO-W, MM, MP, TS, LS: this means, that patients origin from Cottbus (Germany) too?

Reply #4:

The patients originated exclusively from our institution (Poznan (Poland)).
We considered collecting/searching literature as a form of study material provision.
As it was wrong interpretation of this point, the initials of two colleagues were removed.

Changes in the text #4:

Line 427: (III) Provision of study materials or patients: BP, AO-W, MM, MP

Reviewer D

Comment #1:
The paper is nicely written and all the points are well explained, however english language needs some improvement.

Reply #1:
Thank you for your comment. The paper was corrected by a native speaker. His name is in the acknowledgement section.

Changes in the text #1:
All linguistic corrections done by native speaker are in blue.

Comment #2:
We believe that echo data are very important, therefore they should be shown in a dedicated table as well as in the manuscript.

Reply #2:
Preoperative echocardiographic data are shown in a dedicated table (Table 2) and the most important in the ‘Results’ sections.

Changes in the text #2:
All echocardiographic data are shown in Table 2 entitled ‘Preoperative echocardiographic findings’.

Comment #3:
The lower incidence of SAVR procedure in 2020 can be explained not only by the pandemic era occurrence. As a matter of fact the incidence of TAVI procedures is growing rapidly in most experienced hospitals due to several well known aspects (such as TAVI accepted for the low risk patients) independently from the COVID era.

Reply #3:
Of course, that is true. Such comment is in the first passage of the ‘Discussion’ section. However, we think that was not a case in our center.

Changes in the text #3:
The following sentence was added (lines 301-303).
It seems that in our center, the pandemic had more significant impact of a choice of therapeutic option than a global tendency of TAVI promotion. Herein, the only difference regarding therapeutic method rate was found between 2019 and 2020 but not earlier.

Comment #4:
The authors point out the need for delaying elective operations. This statement is in contrast with the total number of operations that have been performed: total aortic valve operation=TAVI+SAVR in the examined periods: 2018=50, 2019=52, 2020[COVID+]=56).

Reply #4:
Probably we were not precise in pointing out the need for delaying elective operations. It referred only to open surgical cases as they need ICU with experienced and highly qualified medical personnel and using deficient (of course during pandemic) devices such as respirators and personal protective equipment. We did show that meeting health care system and social expectations some borderline patients (TAVI/SAVR) were qualified to TAVI. Probably in 2018 or 2019 they would have undergone SAVR. Such comment was also pointed out in the first passage of the ‘Discussion’ section. Moreover, another sentence was also added to the further parts of this section.

Changes in the text #4:
Lines 364-367: […] It is possible that some of the patients on the waiting list with borderline (eg.,moderate or even low risk, with not so many concomitant diseases) indications for TAVI, eventually underwent percutaneous procedures due to aforementioned limitations regarding access to ICU facilities.

Comment #5:

In the section Results the authors only focus their attention on preoperative patients characteristics. Postoperative details are missing. We believe that this is absolutely unacceptable and this section needs major revision.

Reply #5:

Although the first idea of our paper was to present just preoperative patients characteristics, following almost all Reviewers' suggestions or recommendation we did feel obliged to include outcome in our study. This major change resulted in substantial revision in almost all sections of our manuscript.

Changes in the text #5:

The detailed changes in the following sections:

'Abstract'

[…] We assessed if there were any differences regarding patients' clinical profile, applied therapeutic method, procedure complexity and early clinical outcomes.

[…] During the pandemic, a change in applied therapeutic methods and differences in patients' clinical profile did not have an unfavorable impact on in-hospital mortality (2.0% before vs. 3.6% during pandemic) and morbidity. Of note, intubation time and in-hospital stay were significantly shorter ($p<0.05$) in 2020 (4.2 hours and 7.5 days) than in the previous years (7.5 hours and 9.0 days, respectively).

[…] The shift into less invasive treatment method of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes.

'Introduction'

Therefore, the purpose of our cross-sectional study was to determine if the COVID-19 pandemic had any impact on management, the clinical profile and early outcomes of patients treated for severe AS.

'Material and methods'

A subsection entitled '2.5. Postoperative period' has been added

2.5. Postoperative period

The selected individuals after TAVI (with intraprocedural complications or these considered preoperatively as very high risk) and all patients who got SAVR were transferred to the postoperative ICU, intubated and mechanically ventilated.

According to the hospital rules, patients in stable clinical status after ICU stay were further treated at either the cardiac surgery (SAVR) or cardiology (TAVI) ward. The subjects after open surgical operations were usually discharged to rehabilitation centers whereas those following percutaneous interventions usually were sent home directly.

Consequently, the numbering of the subsequent subsections of 'Material and methods' have also been changed (2.5 to 2.6 and 2.6 to 2.7, respectively).

In subsection '2.6. Parameters included' the following text was added:

[…] Postoperative in-hospital course, including mortality and morbidity was also analyzed. Moreover, a length of endotracheal intubation (if applicable), ICU and in-hospital stays were evaluated. Additionally, the following serious adverse events were taken into account:

-myocardial infarction (defined if all conditions such as significant increase in troponin I concentration, ischemic changes in electrocardiogram and new local disturbances in myocardial contractility were fulfilled simultaneously),

-atrio-ventricular block (AVB) requiring permanent pacemaker implantation,

-renal failure treated by means of renal replacement therapy (continuous veno-venous hemodialysis, CVVHD),

-respiratory failure if patients had to be intubated longer than 12 hours or be reintubated,

-stroke (confirmed in neurological (specialist consultation) and imaging examinations (computed tomography or magnetic resonance imaging)),

-bleeding from surgical access (TAVI) or bleeding/tamponade requiring chest re-exploration,

-deep surgical site infection (DSSI) treated with repeat sternal reosteosynthesis (after SAVR),

-peripheral TAVI access serious complications (eg., artery dissection, false aneurysm) if vascular open or intravascular interventions were necessary.

'Results'

3.5. Postoperative course

Overall, short-term mortality defined as all deaths that occurred within the first 30 days following procedure irrespective of patient stay (hospital, rehabilitation center, home) was 2.5% (n=4), two fatal cases in both subgroups. Mortality rate among

COV(-) individuals was 2.0% while 3.6% in COV(+) group (ns). Taking into account a method of aortic valve implantation, single SAVR patients died either in the years 2018-2019 or in 2020 (both had combined procedures, SAVR completed by CABG) whereas all TAVI subjects (n=2) before SARS-CoV-2 pandemic. The reasons of death myocardial ischemia – induced low cardiac output syndrome (LCOS) (n=2; on 3rd and 5th postoperative days) in SAVR group whereas fatal bleeding due to perforation of left ventricle (intraoperative death) and LCOS preceding multi-organ failure (MOF) in TAVI subjects.

The other postprocedural serious adverse events are summarized in Table 4. Of note, the rate of them was comparable in the consecutive years in TAVI group (28% in 2018, 36% in 2019 and 24% in 2020; ns) while in SAVR subset it was significant higher (p=0.048) in 2020 (42%) than in the years 2018-2019 (19%).

Additionally, comparison of intubation time and in-hospital stay revealed their median times for of all patients irrespective of valve implantation technique was significantly shorter in the year of SARS-CoV-2 pandemic than previously (see Figure 2). It probably resulted from higher contribution of TAVI procedures after pandemic outbreak. Detailed analysis of the aforementioned variables of the postoperative course were comparable within both subgroups in the consecutive years (SAVR 2018 = SAVR 2019 = SAVR 2020; TAVI 2018 = TAVI 2019 = TAVI 2020) but notable they were always markedly shorter in TAVI individuals (ie. TAVI 2018<SAVR 2018, TAVI 2019<SAVR 2019, TAVI 2020<SAVR 2020) (see Table 5). As it is stated in the text two additional table 4 and 5 completed presentation of postoperative course analysis.

‘Figures’

Figure 2 was also replaced and the current one refers to early clinical results.

‘Discussion’

Two below paragraphs have been added to ‘Discussion’ section:

Herein, we also observed the changed management with AS patients in the pandemic era did not negatively impact the early clinical outcomes expressed as in-hospital mortality and prevalence of serious adverse events. In our group, overall mortality rate was comparable or slightly higher than in the previously published studies [37, 38]. Contrary to them, in our group of SAVR cases, even one thirds had to undergo simultaneous CABG [17, 18]. The latter one was proved to have unfavorable

influence on both early and late outcomes, particularly in women [39-41]. Moreover, CAD accompanying hypertrophic LV myocardium induced by severe aortic valve stenosis poses a high risk of intraoperative myocardial ischemia. Of note, in both patients who died soon after surgery, preoperative coronary angiography revealed significant lesions that had to be addressed during surgery.

Very important issue during the SARS-CoV-2 pandemic is a limited number of beds with monitoring of vital signs. Therefore, currently all actions resulting in the shortening of in-hospital stay are welcome. We did observe the shortest hospitalization time in 2020, mainly due to an increased rate of TAVI procedures. The latter ones, especially these performed on moderate risk patients and with uneventful postprocedural course, were found to be associated with earlier discharge than after SAVR. Our findings regarding this issue supported the previous reports [17, 18, 42, 43]. Some of them stressed economic aspects of AS treatment [44]. It was showed that more common application of TAVI procedures, in spite of high price of implanted bioprostheses, had important implications in the era of constrained resources with a growing emphasis on reducing health care costs [44].

‘Conclusions’

This shift into less invasive method of treatment of aortic stenosis patients resulted in shortening of in-hospital stay without compromise of short-term outcomes. This strategy fulfilled expectations of health care system during SARS-CoV-2 pandemic.

Comment #6:

Finally, based on my previous considerations, it is somewhat uncertain if the manuscript conclusions could improve our scientific knowledge in aortic valve treatment during COVID 19 pandemic, without any suggested major revisions.

Reply #6:

We hope suggested major revisions led to improved value of our manuscript. We think that good clinical outcomes together with shortening in-hospital stay (the latter one of paramount importance during SARS-CoV-2 pandemic) were possible, at least partially, owing to shift into less invasive technique in AS patient treatment.

Changes in the text #6:

N/A.