Absence of patient-prosthesis mismatch in valve-replacing aortic root surgery using both stentless and stented valved conduits. An institutional retrospective analysis of 40 consecutive patients

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Abstract:

Introduction:

Stentless biological aortic valved conduits have been introduced as an alternative to classical Bentall Operation. The presence of patient-prosthesis mismatch (PPM) in aortic valved conduits remains unclear. Superior hemodynamics have been described for stentless aortic valves but not aortic valved conduits. Possibly, a larger effective orifice area might lead to better outcome and even facilitate later transcatheter valve-in-conduit implantations.

Materials and Methods:

Consecutive patients (n=40) operated for different indications in a single institution between January 2019 and January 2021 (25 months) were retrospectively reviewed. Diagnoses, perioperative risk factors, the Euroscore II (2011), operative technique, short-term outcome and echocardiographic results were analyzed.

Results:

Indications included aneurysm (21/40, 52%) and type A dissection (19/40, 48%) combined with valve pathologies precluding valve preservation. Fourteen stentless biological conduits (10 BioIntegral, 4 Medtronic Freestyle), 20 stented biological self-mounted composite grafts (CE Perimount, Hemashield), and 6 ready-to-use mechanical valved vascular grafts (SJM Masters + Hemashield) were implanted. Euroscore II was higher in the stentless biological and stented biological compared to the mechanical group (15.3 $\pm$ 13.3 vs. 12. 3 $\pm$ 12.0 and 7.9 $\pm$ 6.3, respectively, p=0.28). Body surface area (BSA) was lowest in the stentless group (1.95 $\pm$ 0.23 vs. 2.10 $\pm$ 0.27 and 2.36 $\pm$ 0.49 m^2, respectively, p=0.02). There were no prosthetic valve dysfunctions and no PPM in either groups, with mean gradients below 30 mmHg and EOAI higher than 0.9 cm^2/m^2 (available N=37 and N=30, respectively). Implanted valve diameters were - in relation to body surface area - larger in stentless compared to stented biological, but not mechanical valves (25.4 $\pm$ 2.0 vs. 25.0 $\pm$ 2.1 and 26.0 $\pm$ 1.1, p=0.51). In bio-valves, maximum and mean transvalvular echocardiographic gradients were lower (19.3 $\pm$ 8.3 and 11.6 $\pm$ 6.8 mmHg vs. 20.9 $\pm$ 4.7 and 12.0 $\pm$ 3.1 mmHg) and EOAI (1.30 $\pm$ 0.23 cm^2 per m^2 vs. 1.12 $\pm$ 0.13 cm^2/m^2, p=0.02) higher in stentless compared to stented ones. In mechanical conduits higher gradients (27.2 $\pm$ 12.5 and 16.3 $\pm$ 6.4 mmHg) but also favourable EOAI (1.46 $\pm$ 0.64 cm^2/m^2) were observed (p=0.07). After a mean follow-up of 14 months, still transvalvular gradients were lower and EOAI higher in the stentless vs. the other groups (1.56 $\pm$ 0.73 vs. 1.10 $\pm$ 0.16 vs. 1.10 $\pm$ 0.16 cm^2/m^2, respectively). In total 6 perioperative deaths (1/6 intraoperative, 3/6 in-hospital deaths, 2/6 out of hospital) were observed. There were no surgery-related deaths throughout the postoperative period. One patient died of COVID-19 pneumonia 13 months after surgery.

Conclusions:

PPM seems generally not to be an issue in aortic valved conduit implantation. However, lowest transvalvular gradients and largest EOAI were found in the stentless group. Whether this might further improve patient outcomes and enhance feasibility of valve-in-conduit procedures remains to be awaited.

Introduction:

Stentless fully biological aortic valved conduits have been introduced as an alternative to composite Bentall-Operation and to homograft or autograft replacement of the aortic root as early as in 1990.[1,2] Due to their all-biological nature, their particular use in endocarditis of the aortic valve and root was advocated.[3] Reports of hemodynamical advantages over stented composite biological valved roots have extended indication beyond endocarditis.[4] Data on different stentless valved conduits have been published, particularly for the Freestyle and BioIntegral conduits with good clinical results.[5-8]The latter has undergone modifications in the production process after reports of post-implantation false-aneurysm formation.[9] Alternatively, composite biological aortic valved conduits made of commercially available valve substitutes and vascular synthetic woven grafts have become popular, e.g. with one study reporting excellent results with a re-intervention-free survival of 97.6% after 5 years.[10] However, despite reports on hemodynamic superiority, [11] stentless valved conduits have not replaced their opponents to now. [12] Excellent functional results for stentless aortic valved conduits in patients with small annuli have been demonstrated.[13] In aortic root surgery, studies comparing stented versus stentless valved conduits are missing and the question of patient-prothesis mismatch

(PPM) remains obscure. Recent studies show that both de novo PPM after valve-in-valve procedures [14] and pre-existing PPM[15,16] raise mortality. Any superior effective orifice area of aortic valve substitutes may be of interest in the light of transcatheter valve-in-valve procedures. Low-risk alternatives to re-do surgery particularly after biological valve-replacing aortic root procedures are sought. [17] The present institutional retrospective study was undertaken to rule out the existence of PPM for different forms of Bentall operations under real-life conditions.

Materials and Methods

Ethics approval was granted by the Ethics Committee of the 'Aerztekammer' of the Federal State of Nordrhein-Westfalen, Germany, waiving individual patient consent. A systematic retrospective search was undertaken in the computerized database of our hospital. Consecutive patients with valve-replacing aortic root surgery from January 2019 to January 2021 (25 months). Surgeries were performed for aneurysm, aortic valve insufficiency with anulo-aortic ectasia, or Type A-dissection with aortic root affection. Cases of valve-sparing aortic root surgery were excluded from the analysis, as were cases of aortic valve replacement plus supra-coronary aortic replacement. There were included elective, urgent, emergent and re-do cases, e.g. a re-do case with postoperative aneurysm or a case of paravalvular leak after TAVI. Several patients had concomitant procedures.

Biological valves were generally preferred at an age beyond 60 years. Moreover, it was left at the discretion of the implanting surgeon whether to implant a stentless instead of a stented biological graft, e.g. because of small anulus. Biological stented composite grafts were self-manufactured after sizing of the patient's annulus by using a valve and a vascular graft 5 mm larger than the valve prosthesis. Pre-assembled mechanical grafts were used according to guidelines in younger patients. Sewing technique was either by interrupted or running suture (stentless only). BioIntegral prostheses could be oversized generally by 2 or 4 mm. In patients with aortic arch replacement including frozen elephant trunk procedures, the right axillary artery was cannulated and neuroprotection was achieved by deep hypothermia and selective antegrade cerebral perfusion, as described.[18]

Procedural, clinical, echocardiographic and follow-up data were collected from the charts. Patients were followed by the institutional 'aortic team'.

Data were imported to SPSS Statistics 11.5 for description and analysis. Categorical data are shown as numbers (No.) and percent (%), comparison was performed using the Fisher's exact or chi-square test, where appropriate. When normal distribution was assumed, continous variables were compared as mean +- standard deviation using the Student un-paired t-test. Alternatively, the ANOVA-test was used, where appropriate. For the student's un-paired t-test, the Levene-Test for variance equality was used, which was not significant at >0.05, and thus variance equality was assumed. Body surface area was calculated according to the Dubois formula.

Postoperative gradients and aortic valve area index calculations were usually performed one week postoperatively. Aortic valve area index was calculated with the continuity equation and the preoperative body surface area.

Results:

Table 1 shows demographic data of the surgical study population. Underlying indications were either aneurysm (21/40, 52%) or type A dissection (19/40, 48%) combined with valve deterioration precluding valve repair. There were more type A dissections in the stentless valved conduit group. Connective tissue disease and bicuspid valves were more often seen in the stented valve group. The mechanical valve group was younger in average. Comorbidity analysis showed a higher risk in the stentless group. Euroscore II was highest in the stentless biological group compared to stented biological and mechanical valves (15.3 +- 13.3 vs. 12. 3 +- 12.0 vs. 7.9 +- 6.3, respectively, p=0.28). Moreover, patients receiving stentless conduits were older and their body surface area (BSA) was lowest (1.95 +- 0.23 vs. 2.10 +- 0.27 vs. 2.36 +- 0.49 m^2, respectively, p=0.02).

Table 2 shows operative data. There were more urgent and emergent cases in the stentless group. Fourteen stentless biological conduits (10 BioIntegral, 4 Medtronic Freestyle), 20 stented biological self-mounted composite grafts (CE Perimount, Hemashield vascular prostheses), and 6 ready-to-use mechanical valved vascular grafts (SJM Masters pre-assembled valved conduit) were implanted. Valve diameters were not significantly larger in either group (25.4 +- 2.0 vs. 25.0 +- 2.1 and 26.0 +- 1.1, p=0.51). Vascular tube graft diameters in the biological composite group were chosen depending on valve diameter, following the rule of valve diameter plus 5 mm. Aortic arch replacement was performed in 21/40 patients, consisting of 15 oblique hemiarch replacements, 4 conventional total arch replacements and 2 frozen elephant trunk replacements. More arch replacements and more concomitant procedures were performed in the first two groups leading to longer CPB and cross-clamp times. No significant differences could be observed among groups in terms of consumption of red blood cell or thrombocyte transfusion.

Table 3 shows early clinical results and hemodynamic data of the different valve substitutes. No prosthetic valve dysfunction and no PPM were observed throughout the study period following current definitions (mean gradients < 30 mmHg, all EOAI [?] 0.9 cm^2/m^2).[19] Table 3 shows echocardiographic values in the immediate postoperative (PO) and follow-up period (FUP). FUP examinations took place either in our outpatient clinic or in cardiologists' private practice. Ideally, maximum and mean transvalvular echocardiographic gradients as well as EOAI were measured. Available data are depicted in the table. Stentless valves displayed the lowest transvalvular gradients and the highest calculated EOAI values. Figures 1 and 2 compare EOAI in the PO setting vs. FUP. Notably, this comparison revealed a significantly larger EOAI for the stentless group and the effect lasted throughout the FUP period.

After a mean follow-up of 14.0 months (95% confidence interval: 10.7 – 17.4), 7 cumulative death events were recorded. There were 6 perioperative deaths. Four out of 6 died because of complications and sequelae of type A dissection including malperfusion, cardiogenic shock or multi-organ failure, and 2 died after non-emergent surgery. One of these underwent repair of a giant aneurysm involving the total arch and developed multi-organ failure, the other was operated for a large pseudoaneurysm after previous Bentall operation using a BioIntegral conduit 2 years earlier with underlying Marfan syndrome and died intraoperatively. Thus, an overall perioperative mortality of 15% was observed (6/40, Table 3). The seventh patient died of COVID-19 pneumonia 13 months after an uneventful aortic root surgery. Kaplan-Meier analysis shows no mortality beyond the perioperative period except for the COVID-19 case. (Figure 3)

Neurological symptoms were present in 4 patients. One of these presented preoperatively with a fluctuating unconsciousness and developed a postoperative 'coma vigile' due to ischemic stroke and malperfusion; he died perioperatively. In addition there were 3 perioperative strokes (all survivors), 2 disabling strokes (hemiparesis, paraplegia) and one with minor locomotor disturbances.

During follow-up, no valve- or surgery-related postoperative adverse events or deaths were identified among the study population.

Conclusions:

The present institutional study reviews operative results of 40 different consecutive valve-replacing aortic root techniques over a 25 months period. Comparison with the literature reveals that peri-operative mortality for elective Bentall operation and for acute type A dissection in representative studies is reported to be as high as 6% and 17%, respectively. [20,21] Considering older patient age, pronounced comorbidities and more complex procedures in our study cohort, in-hospital mortalities of 5% for aneurysms and 15% for the whole population appear acceptable. Echocardiographic analysis revealed that the use of different composite prosthetic valves and aortic substitutes was totally free of PPM. Data on PPM for patients receiving aortic valved conduits are virtually missing. Particularly in small patients with low body surface areas there are no recommendations on which type of prosthesis to use. As mentioned before, a higher effective orifice area for stentless valves has been described for ordinary aortic valve replacement; for aortic valved conduits, however, the situation remains unclear. Despite low numbers, our institutional data show that PPM seems not to be an issue at all in Bentall operation. It can be speculated that the technique of valve-replacing root surgery by itself helps oversizing the anulus thus eliminating PPM.

In the present study, EOAI in stentless conduits were similar to the excellent values of stentless aortic valve replacements reported by the Toronto group, [22] reaching average values around 1.30 cm^2/m^2, which means that the "stentless factor" can be appreciated also in aortic valved conduits. On the other hand, we did not find PPM in any of the valve prostheses used, nor did we notice any valve dysfunction of any type during the observation period. Thus, a clear recommendation in favour of stentless prostheses cannot be derived from the present data.

Another key point should be addressed. As we know from recent meta-analyses, outcome after valve-in-valve procedures is negatively affected by PPM and pre-existing PPM. [14] When open re-do surgery represents a major risk, such as after Bentall operation, valve-in-conduit might represent a treatment alternative, particularly at higher comorbidity and age. A larger EOAI in a stentless valved conduits might further enhance the up-sizing effect inherent to Bentall operation, thus facilitating later transcatheter valve-in-conduit interventions. Further studies might be necessary to elucidate this.

We re-operated a patient because of a huge false aneurysm of the neo-aortic root 2 1/2 years after BioIntegral implantation for acute type A dissection and Marfan syndrom. The underlying pathology could not be linked to any presence of endocarditis. The company recommends using interrupted sutures for the basal anastomosis and to avoid use of two-component sealants.

There are drawbacks when arguing in favour of stentless conduits. First, there is limited reported evidence for feasibility and technical safety for valve-in-conduit interventions. Successful valve-in-conduit procedures have been reported in a small series e.g. for the Medtronic Freestyle. [23] Second, in the absence of contraindications to anticoagulation, the mechanical conduit remains a valuable alternative in terms of hemodynamic performance.[12]

Summarizing, the present study showed excellent hemodynamic performance and excluded PPM for all types of valved conduits used. EOAI measurements revealed advantages for stentless bio-conduits but outside the range of PPM. Therefore, no clear recommendation in favour of stentless conduits can be given. Whether larger EOAI among stentless conduits can translate into better patient outcomes and can enhance feasibility of valve-in-conduit procedures remains to be awaited.

References

1. David TE, Pollick C, Bos J. Aortic valve replacement with stentless porcine aortic bioprosthesis. *J Thorac Cardiovasc Surg.*1990;99(1):113-118.

2. Carrel TP, Berdat P, Englberger L, et al. Aortic root replacement with a new stentless aortic valve xenograft conduit: preliminary hemodynamic and clinical results. *J Heart Valve Dis.*2003;12(6):752-757.

3. Siniawski H, Grauhan O, Hofmann M, et al. Aortic root abscess and secondary infective mitral valve disease: results of surgical endocarditis treatment. *Eur J Cardiothorac Surg.*2005;27(3):434-440.

4. Sherrah AG, Jeremy RW, Puranik R, et al. Long Term Outcomes Following Freestyle Stentless Aortic Bioprosthesis Implantation: An Australian Experience. *Heart Lung Circ.* 2016;25(1):82-88.

5. De Paulis R, Nardi P, De Matteis GM, Polisca P, Chiariello L. Bentall procedure with a stentless valve and a new aortic root prosthesis.*Ann Thorac Surg.* 2001;71(4):1375-1376.

6. Bach DS, Kon ND, Dumesnil JG, Sintek CF, Doty DB. Ten-year outcome after aortic valve replacement with the freestyle stentless bioprosthesis. *Ann Thorac Surg.* 2005;80(2):480-486; discussion 486-487.

7. Mehdiani A, Sorokin VA, Sule J, et al. Mid-term single-center outcomes of BioIntegral compared to Freestyle aortic conduit implantation. *J Cardiovasc Surg (Torino).* 2020;61(4):512-519.

8. Puehler T, Freitag-Wolf S, Friedrich C, et al. Outcomes of Patients after Implantation of the Pericardial All-Biological Valve No-React Aortic Conduit (BioIntegral) for Root Replacement in Complex Surgical

Procedures. *Thorac Cardiovasc Surg.* 2020;68(4):301-308.

9. Reineke DC, Kaya A, Heinisch PP, et al. Long-term follow-up after implantation of the Shelhigh(R) No-React(R) complete biological aortic valved conduit. *Eur J Cardiothorac Surg.* 2016;50(1):98-104.

10. Gaudino M, Lau C, Munjal M, Avgerinos D, Girardi LN. Contemporary outcomes of surgery for aortic root aneurysms: A propensity-matched comparison of valve-sparing and composite valve graft replacement. *J Thorac Cardiovasc Surg.* 2015;150(5):1120-1129 e1121.

11. Cohen G, Zagorski B, Christakis GT, et al. Are stentless valves hemodynamically superior to stented valves? Long-term follow-up of a randomized trial comparing Carpentier-Edwards pericardial valve with the Toronto Stentless Porcine Valve. *J Thorac Cardiovasc Surg.*2010;139(4):848-859.

12. McCarthy FH, Bavaria JE, Pochettino A, et al. Comparing aortic root replacements: porcine bioroots versus pericardial versus mechanical composite roots: hemodynamic and ventricular remodeling at greater than one-year follow-up. *Ann Thorac Surg.* 2012;94(6):1975-1982; discussion 1982.

13. Tavakoli R, Auf der Maur C, Mueller X, et al. Full-root aortic valve replacement with stentless xenograft achieves superior regression of left ventricular hypertrophy compared to pericardial stented aortic valves. *J Cardiothorac Surg.* 2015;10:15.

14. Pibarot P, Simonato M, Barbanti M, et al. Impact of Pre-Existing Prosthesis-Patient Mismatch on Survival Following Aortic Valve-in-Valve Procedures. *JACC Cardiovasc Interv.* 2018;11(2):133-141.

15. Thandra A, Abusnina W, Jhand A, et al. Valve-in-valve transcatheter aortic valve replacement versus redo surgical valve replacement for degenerated bioprosthetic aortic valve: An updated meta-analysis comparing midterm outcomes. *Catheter Cardiovasc Interv.*2021;97(7):1481-1488.

16. Sa M, Van den Eynde J, Simonato M, et al. Valve-in-Valve Transcatheter Aortic Valve Replacement Versus Redo Surgical Aortic Valve Replacement: An Updated Meta-Analysis. *JACC Cardiovasc Interv.*2021;14(2):211-220.

17. Esaki J, Leshnower BG, Binongo JN, et al. Reoperative aortic root replacement: Outcome in a contemporary series. *J Thorac Cardiovasc Surg.* 2017;154(3):800-808 e803.

18. Peterss S, Pichlmaier M, Curtis A, Luehr M, Born F, Hagl C. Patient management in aortic arch surgerydagger. *Eur J Cardiothorac Surg.*2017;51(suppl 1):i4-i14.

19. Pibarot P, Dumesnil JG. Prosthesis-patient mismatch: definition, clinical impact, and prevention. *Heart.* 2006;92(8):1022-1029.

20. Mookhoek A, Korteland NM, Arabkhani B, et al. Bentall Procedure: A Systematic Review and Meta-Analysis. *Ann Thorac Surg.*2016;101(5):1684-1689.

21. Lee TC, Kon Z, Cheema FH, et al. Contemporary management and outcomes of acute type A aortic dissection: An analysis of the STS adult cardiac surgery database. *J Card Surg.* 2018;33(1):7-18.

22. Borger MA, Carson SM, Ivanov J, et al. Stentless aortic valves are hemodynamically superior to stented valves during mid-term follow-up: a large retrospective study. *Ann Thorac Surg.* 2005;80(6):2180-2185.

23. Reich H, Roselli EE. Defining the Limits of Valve-in-Valve Transcatheter Aortic Valve Replacement for Degenerated Freestyle Bioprosthesis. *Ann Thorac Surg.* 2020;110(6):1957-1958.

Tables:

Table 1: Demographic data

Table 2: Operative data

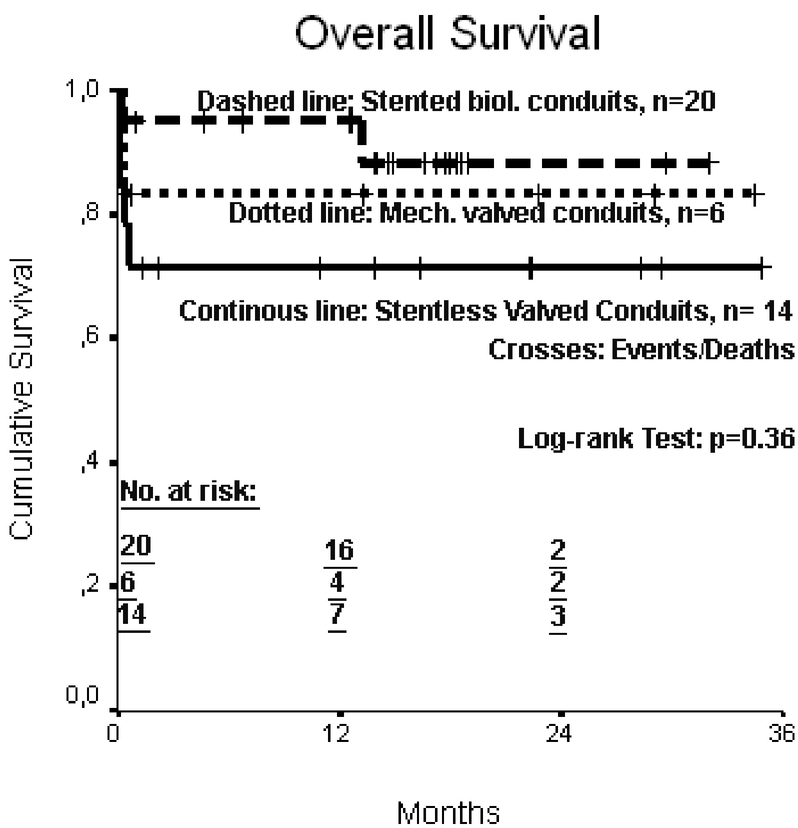
Table 3: Echocardiographic results and outcome

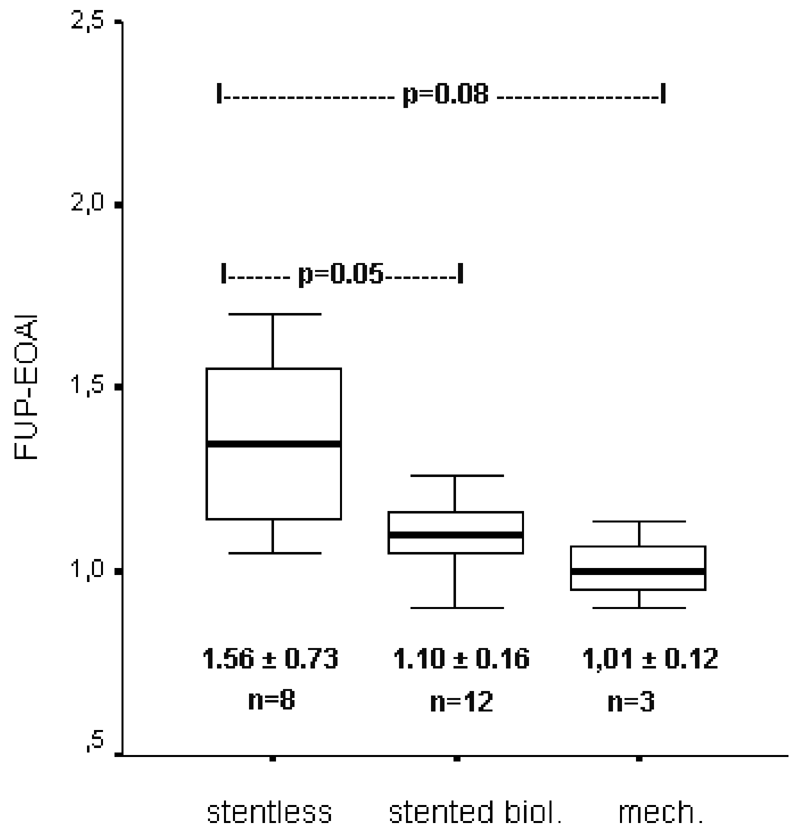
Figure Legends:

Figure 1: Stem and leaf plot of postoperative effective orifice area index (PO-EOAI) in available postoperative echocardiographic measurements (n=30). One-Way ANOVA tests for calculation of p value.

Figure 2: Stem and leaf plot of follow-up effective orifice area index (FUP-EOAI) in available postoperative echocardiographic measurements (n=23). One-Way ANOVA tests for calculation of p value.

Figure 3: Kaplan-Meier plot of univariate overall survival analysis of different prosthetic groups.




2,5
2,0
1,5
1,0
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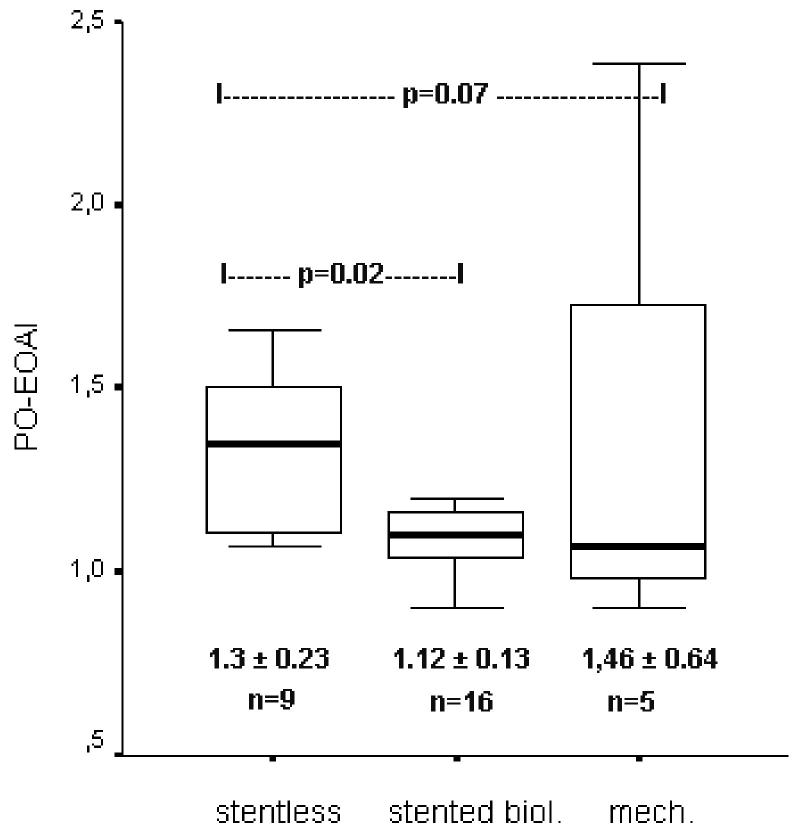
FUP-EOAI
I------------------ p=0.08 ------------------I
I------- p=0.05--------I
1.56 ± 0.73
n=8
1.10 ± 0.16
n=12
1,01 ± 0.12
n=3
stentless
stented biol.
mech.



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