
Peer Review File

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Reviewer A

This is an interesting retrospective review of pediatric patients who undergo right ventricular outflow tract reconstruction using a locally available bovine jugular vein valved conduit (Balance BJVC). There are several typos using the formal name Balance (line 51, 224). A possible additional typo is in line 324. Is this supposed to say "conduit dysfunction?" Also, in line 167, the HTK solution may need to be expanded and not abbreviated here.

Reply 1: **The typos have been corrected and the name of HTK solution has been expanded to the whole name.**

Changes in the text: **Line 55, 248. Line 190.**

There are several questions and desired clarifications that come to mind with this manuscript. Under the Key Findings and "What is the implication...", the authors mention "optimizing the conduit preparation technique." It is not clear what is meant by this statement, and it is not addressed within the discussion section of the manuscript.

Reply 2: **Based on our investigation, the Chinese local production BJVC can match most of the clinical requirements. To extend its durability, it is still needed to be improved on the treatment process, such as anti-calcification, non-glutaraldehyde based collagen crosslink, even the application of tissue engineering techniques.**

Changes in the text: **L421-424.**

Another question is the authors' distinction between conduit dysfunction and conduit failure. Qualitative and quantitative data for conduit dysfunction are given, but not for conduit failure. What determines conduit failure? The cardiologist's recommendation for surgical replacement over transcatheter intervention? Some studies define conduit failure as the need for any intervention. Do all patients who have conduit failure start as having conduit dysfunction and then progress to failure? One patient had failure but underwent balloon dilation - was this intervention inadequate? Did none of the other patients have transcatheter interventions first before being deemed conduit failure? If not, is there an explanation for this? It looks like failure not related to IE was all by stenosis (not regurgitation) so presumably could be candidates for transcatheter balloon dilation or stenting.

Reply 3: **The definition of conduit failure was not described in the paper. In our clinical practice, we define it as severe stenosis (pressure gradient \geq 80mmHg), or severe regurgitation (greater than grade3+), the re-intervention of surgical operation or transcatheter intervention is necessary, including balloon dilation or stent implantation. Conduit failure is defined by severe structure disease lesion, which has nothing to do with cardiologist's recommendation on surgical replacement or transcatheter intervention. With dysfunction of the conduit, transcatheter intervention is mostly more effective. However, any further approachment can not define the status of the conduits. We do think all patients who have conduit failure start as having conduit dysfunction and then progress to failure. Actually, as clinical doctors, we prefer more active transcatheter intervention treatment. As we describe in (L319-321), "A total of 28 reinterventions were performed in 26 children". We also mentioned "approximately 90% of**

patients were free of bovine jugular vein conduit (BJVC) failure at 5 years after implantation due to aggressive transcatheter intervention” in key founding. Additionally, we think the balloon dilation is not enough for conduit failure, to which extend the conduit has to be taken out and replaced. Whatever, the clinical decision is made by many other factors, including the patients desire and their economic level.

Changes in the text: L159-162.

The authors divided their cohort into conduits 12-14 mm and 15-17 mm. Was there are reason for choosing this cut-off?

Reply 4: In the Discussion section, we mentioned that the smaller diameter conduits (12-14 mm) had higher risk on dysfunction and failure (L369-370).

Changes in the text: No.

The authors referenced several previous studies looking at the use of bovine jugular veins in other cohorts. Another study that is similar to this one is by Zhang et al, Mid- to long-term outcomes of bovine jugular vein conduit implantation in Chinese children, J Thorac Dis 2017; 9:1234-1239. There are some differences, including how Zhang et al define conduit failure as well as having fewer patients, but with longer follow up. The authors should consider describing how their study is novel compared to this previous study.

Reply 5: Based on our investigation, the incidence of infective endocarditis (IE) is not such high (5.3%). On the other hand, under the consent of family dependents, more active transcatheter treatment will be adopted if the dysfunction of the conduit was diagnosed. Therefore, the risk of conduits decay after 5 years implantation is comparatively low even though the patients in the cohort are younger (36.2% patients are younger than 12 months) and the incidence of conduits dysfunction is higher.

Changes in the text: L410-420.

Reviewer B

1) First, the title needs to indicate the study participants and the clinical research design of this study, i.e., a retrospective cohort study.

Reply 1: We have changed the title to “Medium-term outcomes of bovine jugular valved conduits for right ventricular outflow tract reconstruction: a retrospective cohort study from China”

Changes in the text: L3-4.

2) Second, the **abstract** needs some revisions. The background did not indicate the knowledge gap on the efficacy of BJVC and the clinical needs for this research focus. In the methods, please describe how the patients were selected, how their baseline characteristics were measured, how these patients were followed, and how the outcomes were measured. Because of no a control group receiving standard treatment, the authors need to consider to town done the current conclusion and have comments for the clinical implications of the findings.

Reply 2: We revised the abstract based on the suggestion above. Because our clinical data shows

that the BJVC can totally match the treatment requirement, the conclusion is fully objective.
Changes in the text: L50-79.

3) Third, the **introduction** needs to review what has been known on the efficacy and safety of BJVC including international studies and analyze the knowledge gaps. It is also necessary to describe the clinical needs for the middle-term outcomes of BJVC, not early and long-term outcomes. Please also clearly define medium-term outcomes.

Reply 3: **The Introduction has been revised accordingly. The purpose of this study is to evaluate the function of the BJVC conduit, the early deaths is usually not due to the conduits but other specific reasons, so the early deaths as well as early follow-up loss cases are excluded in the statistics. So far, the follow-up data is in mid-term time span, we will keep follow-up this cohort and report long term data which is also very important for the conduit as well as the treatment.**
Changes in the text: L97-110.

4) Fourth, in the methodology of the main text, please accurately describe the clinical research design, sample size estimation, and follow up details of this study. In statistics, please describe the groups to be compared by using t test or other tests, as well as the purposes of the Cox regression analysis. Please ensure $P < 0.05$ is two-sided.

Reply 4: **This study is retrospective analysis in single center. All pediatric patients undergoing RVOT reconstruction using Balance BJVC in our center from January 2018 to December 2020 were enrolled in this study. (line 128-135.) Follow up details were described in "Follow-up and reintervention" section (L200-207) . We have revised accordingly.**

Changes in the text: L211-216.

Reviewer C

1. The information of Ref. 8 in the main text differed from the information in the reference list. Please revise.

Patel and **Brown** et al. reported the freedom from BJVC explantation was 53% at 5 years and 15% at 10 years for infants **(8)**.

Ref. 8 **Patel** PM, Tan C, Srivastava N, et al. Bovine Jugular Vein Conduit: A Mid- to Long-Term Institutional Review. World J Pediatr Congenit Heart Surg 2018;9: 489-495.

Reply: We have revised.

2. Table 1

We suggest deleting the pointed "(n, %)" and indicate how the data are presented in Tables in the legend. For example, Data are presented as median (interquartile range) or number (%).

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676 **Table 1** Patient demographics and operative procedures ↵

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Demographic ↵	Patients (n, %) ↵
Gender (M/F) ↵	51/43 ↵
Median age at implant (month) ↵	22 (2–168) ↵
Age less than 12 months ↵	34 (36.2) ↵
Median weight (kg) ↵	10.8 (3.8–40.0) ↵
Main diagnosis, n (%) ↵	↵
Aortic cross-clamp time (min) ↵	74.5 (22–193) ↵
Cardiopulmonary bypass time (min) ↵	202 (33–657) ↵
Ventilation time (hour) ↵	71.5 (1–2,323) ↵
ICU stay time (day) ↵	6 (2–97) ↵

Reply: We have revised.

3. ALL abbreviations used in each table/figure or table/figure description should be defined in a footnote below the corresponding table/figure. For example, PA, VSD, MAPCA, RVOT in Table 1. Please check all figures/tables and provide correspondingly.

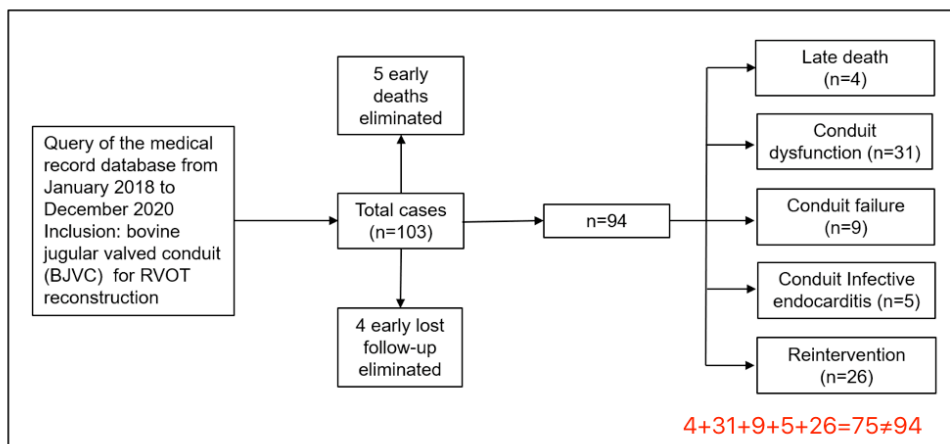
Reply: We have revised.

4. Figure 1

The data looks confusing. Please check and revise.

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653 **Figure 1** Research design map. RVOT, right ventricular outflow tract. ↵

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Reply: We have revised.