Perioperative outcomes of paediatric congenital cardiac surgery in Johannesburg, South Africa

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the Degree of Master of Medicine in the branch of Anaesthesiology

Johannesburg, 2024

Declaration

I, Prathap Sarma, declare that this Research Report is my own, unaided work. It is being submitted in partial fulfilment of the requirements for the Degree of Master of Medicine in the branch of Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

12 December 2024

Abstract

Background: Congenital cardiac diseases are the commonest congenital birth defects with children undergoing surgery at increased risk of mortality. Outcomes following congenital cardiac surgery in children has been well documented in high-income countries for many years, but little is known from the African continent.

Aim: The aim of this study was to determine factors associated with perioperative mortality in patients that underwent congenital cardiac surgery at an academic institution.

Methods: This retrospective cross-sectional study was conducted at Charlotte Maxeke Johannesburg Academic Hospital spanning a period of 12 years (2006-2017). The surgical, ICU, and anaesthetic records of patients that underwent surgery were reviewed. The records of all congenital cardiac disease paediatric patients undergoing surgical repair were reviewed. Associations between demographic, surgical and other factors were sought with mortality. A multivariable regression analysis was performed for the factors which had p-values of 0.1 and less in the univariable regression analysis. A Cox regression analysis was performed for mortality over time. All hypothesis testing accepted a p-value of <0.05 as statistically significant.

Results: There was an 11% (188/1701) in-hospital mortality rate overall. Patients that died were primarily younger, 0·33 years (IQR 0·13 - 1·25), had lower median weight of 5kg (IQR 3·45 – 8·20), longer cardiopulmonary bypass (179 min) (IQR 16·0 - 272·5) and aortic cross clamp (82·5min) (IQR 35.0-139.0) times. Palliative surgeries had the highest mortality rate with 41% of all mortalities coming from this category.

Cardiopulmonary bypass time ($p < 0{\cdot}001$), ICU length of stay ($p < 0{\cdot}001$), aortic cross clamp time ($p = 0{\cdot}001$), days on the ventilator ($p < 0{\cdot}001$), and the STAT 2020 mortality score ($p = 0{\cdot}04$) were independently predictive of perioperative all-cause in-hospital mortality in a multivariable regression model. The model yielded an area under the curve of 90%.

Conclusion: Perioperative mortality following congenital cardiac surgery was higher in our study group compared to high income countries but it was similar to that of other low-middle income countries.

Acknowledgements

I would like to thank the following people for their contribution to this research report:

Prof. Palesa Motshabi-Chakane, the supervisor, for her constant guidance, motivation and dedication.

Dr. Palesa Mogane, Dr Kathy Vanderdonck and Dr Moses Kebalepile for assisting in the fine-tuning of the research, their attention to detail and research insight.

To my wife, Sreesudha Sarma, whose boundless support and unwavering love have been the cornerstone of this project and my greatest source of strength.

To Appa and Amma, whose limitless encouragement and steadfast belief in me have been my greatest inspiration throughout this journey.

To my son, Hridhay, for filling my life with joy.

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Statement

The Research Report consists of the author's guidelines, draft article, study proposal, and annexures. The study proposal is included for background reference and is not for examination.

The formatting of this Research Report complies with the University of the Witwatersrand's Style Guide for Theses, Dissertations and Research Reports. The formatting of the draft article complies with the author's guidelines of Anesthesia & Analgesia, the journal to which it is intended to be submitted and may therefore differ from the rest of the Research Report. These differences include the referencing style, margins, font, numbering of figures and tables, and word count.

Section 1: Author's guidelines – Anesthesia & Analgesia

ANESTHESIA & ANALGESIA®

We greatly appreciate your interest in submitting your manuscript to *Anesthesia & Analgesia*. Our goal is to provide authors with a thorough yet timely review of their submissions. Authors will be updated as to the status of their manuscript via Editorial Manager: if you have not had a response within 8 weeks, please contact the Journal Editorial Office.

Notice: The **Instructions for Authors** for *Anesthesia & Analgesia* have been further revised. New submissions should be prepared according to the Instructions that follow. Failure to do so may result in your submission being returned without review.

This now current Version 7.4 of these Instructions for Authors replaces the earlier Version 7.3.

Initial Submission: As of October 1, 2023, *Anesthesia & Analgesia* is adopting a progressive, "open format" for all initially submitted manuscripts (referred to as the R0 version). Authors may, if they wish, submit their manuscript in any style (font, spacing, reference style) of their choosing, although the Journal style is preferred. Authors may submit their initial R0 manuscript as a single file, or multiple files via Editorial Manager. The article type must be specified according to the accepted types listed below. The article subheadings and word limits must also be adhered to in the initial R0 manuscript: "open" refers only to the formatting requirements.

Submitting in the Journal style will however be mandatory if the manuscript is potentially acceptable for publication, so a revised version (termed R1) will need to fully follow the details of the style guide below, in Section 7: Manuscript Preparation Requirements, and the revision may be returned if it does not.

As of April 17, 2023, *Anesthesia & Analgesia* is accepting Research Letter submissions. Authors of a Research Letter are expected to adhere to the requirements in Section 8: Editorial, Ethical and Legal Requirements, specifically including those regarding human subjects research, and if applicable in their country, the use and reporting of protected health information (PHI).

As of October 1, 2023, *Anesthesia & Analgesia* is accepting Video in Clinical Anesthesia submissions. Details are provided below.

As of April 1, 2024, *Anesthesia & Analgesia* is no longer accepting Book and Multimedia Review submissions.

Authors seeking to submit to *A&A Practice* (formerly *A&A Case Reports*) can find its separate *A&A Practice* Instructions for Authors and submit their papers through the *A&A Practice* Editorial Manager Submission Site.

***A&A Practice* remains fully editorially aligned and operationally integrated yet distinct from *Anesthesia & Analgesia*.**

Mission and Scope

Anesthesia & Analgesia exists for the benefit of patients under the care of health care professionals engaged in the disciplines broadly related to anesthesiology, perioperative medicine, critical care medicine, and pain medicine. The Journal furthers the care of these patients by reporting the fundamental advances in the science of these clinical disciplines and by documenting the clinical, laboratory, and administrative advances that guide therapy. *Anesthesia & Analgesia* seeks a balance between definitive clinical and management investigations and outstanding basic scientific reports. The Journal welcomes original manuscripts containing rigorous design and analysis, even if unusual in their approach.

Authors are encouraged to read this editorial, which describes some of the previous changes to the editorial philosophy of *Anesthesia & Analgesia*: Pittet JF, Vetter TR. Continuing the Terra Firma and Establishing a New EQUATOR for *Anesthesia & Analgesia*. Anesth Analg. 2016;123(1):8-9.

Authors are strongly encouraged to adhere to the fundamentals of English grammar, syntax, punctuation, and composition.

Authors are encouraged to read this excellent synopsis on the fundamentals of writing a research report: Sessler DI, Shafer S. Writing Research Reports. *Anesthesia & Analgesia*. 2018;126(1):330-337.

If a paper is poorly written and thus difficult to understand, it will likely **not** receive as favorable a review, despite presenting strong science and/or novel information. If indicated, please consider using a Language Editing Service (see below) to address this issue before your initial submission.

Anesthesia & Analgesia Instructions for Authors

Anesthesia & Analgesia has specific **Instructions for Authors** for submitting articles invited as resubmissions after initial review, which are found below. We strongly encourage all authors to read these instructions completely and carefully, and to prepare their manuscripts in accordance with these instructions.

Revised articles that are not submitted in accordance with our instructions may be returned for revision prior to further peer-review.

Occasionally, authors will be asked by the Journal Editorial Board to resubmit their work as a different article type, which can be done by addressing any initial peer reviewer comments and choosing the new article type in Editorial Manager at the time of manuscript resubmission.

Any changes (additions or deletions) of authors will need to be justified and clearly communicated. See below, **Section 8.A. Role of Authors and Contributors**.

The Journal Editor-in-Chief or other Editorial Board members do not routinely respond to unsolicited manuscript pre-submission inquiries or proposals. Authors are encouraged instead to submit their complete, initial manuscript to the Journal for peer review.

Questions?

If you have a question specifically for the Editor-in-Chief, Dr. Jaideep Pandit, please email him at jpandit@iars.org, or you can contact the Deputy Editor-in-Chief, Dr. Thomas Vetter, at thomas.vetter@austin.utexas.edu.

If you have questions about these submission instructions, or our Journal manuscript processing in general, please contact the **Editorial Office** via editor@anesthesia-analgesia.org

Manuscripts may only be submitted via the Editorial Manager online submission system:
Submit your manuscript to *Anesthesia & Analgesia* here.
Submit your manuscript to *A&A Practice* here.

Download a PDF version of the full Instructions for Authors of *Anesthesia & Analgesia*

INSTRUCTIONS FOR AUTHORS

SECTION 1: *ANESTHESIA & ANALGESIA* ARTICLE TYPES (Back to Contents): Each is described in detail below.

DESCRIPTIONS OF SPECIFIC ARTICLE TYPES

Anesthesia & Analgesia

Original Research Report (Back to Top)

- An **Original Clinical, Health Services, or Educational Research Report** describes an investigation that focuses on the clinical practice of anesthesiology, perioperative medicine, critical care medicine, or pain medicine. They span the spectrum of patient-reported outcomes, clinical effectiveness, quality and performance improvement, patient safety, health services delivery, dissemination and implementation science, health policy, healthcare economics, population health, and education.
- An **Original Laboratory Research Report** describes an investigation that focuses on an aspect of basic science related to anesthesiology, perioperative medicine, critical care medicine, or pain medicine. They span the spectrum of cell biology, immunology, neurobiology, biochemistry, pharmacology, microbiology, and genetics; or are bench studies of equipment.
- The components of an **Original Research Report** manuscript should include (see details below):
  - Title Page
  - Structured Abstract with no more than **400 words**.
  - "Key Points" summary (only for manuscript revisions; not necessary for initial submission): describing the Research Question, Findings, and Meaning, each composed of **one sentence**.
  - Four sections: Introduction, Methods, Results, and Discussion (see details below).
- An Original Research Report can have no more than **12 listed authors**. Other persons may be listed as collaborators in an online supplement: see authorship criteria below.
- The Introduction section should be focused and contain no more than **400 words**. The Introduction succinctly describes, in a series of short paragraphs, the significance of the topic, pertinent background, rationale for the study, *a priori* study aims or objectives, and primary study hypothesis, and if appropriate, secondary study hypothesis.

- The Discussion section should also be focused and contain no more than **1,000 words**. A useful structure for the Discussion, which could form subheadings if desired: (a) summary of main findings in the context of the hypothesis presented in the Introduction (this is not a repeat of the results, but a sentence or two that relates the main findings to the research question); (b) comparison with other work (e.g., how the results are similar to or different from previous results); (c) limitations of the study and/or how any challenges were addressed or overcome; (d) clinical and/or scientific implications; (e) suggestions for further work, which should avoid general phrases like "more studies are needed."
- An Original Research Report contains up to **4,000 words** (not counting the Abstract and references)
- References should be used sparingly. While recognition of previous work is understandable, and the main points in the argument should be supported with references, use of multiple references to justify a single point is discouraged. It is expected that the manuscript will not have more than **40 references**, and more than this number will require explanation in the cover letter and/or justification during the review process. Authors should be prepared to reduce the reference count on editorial direction in any revision.
- An Original Report contains up to **6 tables and/or figures**. Online supplemental material can be provided when appropriate.
- Further resources:
  - Study Reporting Requirement (EQUATOR)
  - Study Reporting Requirement for Animal Studies (ARRIVE)
  - Instructions for Manuscript preparation
  - Instructions for Figure preparation
  - Instructions for Table preparation
  - Instructions for Supplemental Material

Narrative and Systematic Review Article (Back to Top)

- A **Narrative Review Article** or **Systematic Review Article** synthesizes previously published material into an integrated presentation of the current understanding of a topic.
- A Narrative Review can be either **focused** or **comprehensive**, based on its topic and scope.
- A Narrative Review Article should describe aspects of a topic about which scientific and evidence-based consensus exists, as well as aspects that remain controversial and are thus topics for ongoing and future research.
- For a **Systematic Review**, a formal strategy to search and to critically evaluate the medical literature should be applied and well-described. Such explicit methods are used in a **Systematic Review** to minimize bias in its content and findings.
- A Narrative or Systematic Review can have no more than **12 listed authors**. Other persons may be listed as collaborators in an online supplement: see authorship criteria below.
- All such Review articles include a Title Page and an unstructured Abstract with no more than **400 words**.
- The Introduction section should be focused and contain no more than **400 words**.
- A Narrative or Review Article contains up to **5,000 words** (not counting the Abstract and references), **100 references**, and **6 tables and/or figures**. Online supplemental material can be provided when appropriate.
- Further resources:
  - Study Reporting Requirement(EQUATOR)
  - Instructions for Manuscript preparation
  - Instructions for Figure preparation
  - Instructions for Table preparation
  - Instructions for Supplemental Material

Meta-Analysis (Back to Top)

- A Meta-Analysis is a separate submission type to a Systematic Review Article.
- A Meta-Analysis includes a Title Page and structured Abstract of no more than **400 words**.
- A "Key Points" summary will be required in any revision, which describes the Question, Findings, and Meaning, each composed of **one sentence**.
- A Meta-Analysis can have no more than **12 listed authors**. Other persons may be listed as collaborators in an online supplement: see authorship criteria below.
- These manuscripts are divided into four sections: Introduction, Methods, Results, and Discussion.
- The Introduction section should be focused and contain no more than **400 words**.
- The Discussion section should also be focused and contain no more than **1,000 words**.
- A Meta-Analysis contains up to **5,000 words** (not counting the Abstract and references), **150 references**, and **6 tables and/or figures**. Online supplemental material can be provided when appropriate.
- Further resources:
  - Study Reporting Requirement (EQUATOR)
  - Instructions for Manuscript preparation
  - Instructions for Figure preparation
  - Instructions for Table preparation
  - Instructions for Supplemental Material

Editorial (Back to Top)

- An **Editorial** is *solicited* by the Editorial Board and either provides an editorial perspective on an article published in the Journal, or expresses the general policies or opinions of the Journal Editorial Board. If an Editorial is intended to provide an expert perspective on an article or topic published in the Journal, it is typically solicited from reviewer(s) who provided unusually thoughtful insight during the peer-review process, and which the Editors believe should be shared with the Journal readership.
- An Editorial can have no more than **4 listed authors**. No additional collaborators are permitted, but individuals may be listed in acknowledgements.
- An Editorial includes a Title but not an Abstract. The title of Editorial articles should be descriptive of the issues being discussed. It can be entertaining and eye-catching, but not so vague as to apply to anything (e.g., avoid overly general titles like "A Stitch in Time" or "Here We Are Again", which could refer to any topic). Declaratory titles or instructions should be avoided.
- An Editorial contains up to **3000 words** (not counting the references),**20 references**, and occasionally **1 table and/or 1 figure**.
- Further resources:

- Instructions for Manuscript preparation
- Instructions for Figure preparation
- Instructions for Table preparation
- Instructions for Supplemental Material

The Open Mind (Back to Top)

- **The Open Mind** is a unique forum for thoughtful, scholarly, and preferably well-referenced perspectives. The Open Mind is intended to stimulate lively yet civil discussion. It is a forum for (a) challenging myths or dogma and/or (b) proposing new approaches or solutions to an important issue facing the anesthesiology community.
- Presentation of experimental or descriptive data collection and reporting are not permitted with The Open Mind submission.
- An Open Mind submission can have no more than **4 listed authors**. No additional collaborators are permitted, but individuals may be listed in acknowledgements.
- A submission to The Open Mind includes a Title Page but not an Abstract.
- The Open Mind contains up to **3,000 words** (not counting the references), **20** references, and up to **3 tables and/or figures**.
- Further resources:
  - Instructions for Manuscript preparation
  - Instructions for Figure preparation
  - Instructions for Table preparation
  - Instructions for Supplemental Material

Special Article (Back to Top)

- A **Special Article** is intended for when authors occasionally seek to publish a scholarly manuscript that does not fit one of the other above article types.
- A **Special Article** can also be invited by the Editorial Board to examine a specific novel topic.
- Specific subtypes of Special articles include:
  - Clinical Practice Guideline, Consensus Statement, Position Statement, and Practice Alert
  - Statistical Grand Rounds
- A Special Article should not present primary or experimental data collection or comparative data analyses of groups, but references to the data of others or in the public domain may be appropriate.
- A Special Article can have no more than **12 listed authors**. Other contributors may be listed as collaborators in an online supplement.
- A Special Articles include a Title Page and an unstructured Abstract with no more than **400 words**.
- A Special Article contains up to **5,000 words** (not counting the Abstract and references), **50 references**, and **6 tables and/or figures**.
- Further resources:
  - Instructions for Manuscript preparation
  - Instructions for Figure preparation
  - Instructions for Table preparation
  - Instructions for Supplemental Material

Research Letter (Back to Top)

- A **Research Letter** is a concise, focused communication that conveys either (a) preliminary findings of an investigation with novel and potentially important, but limited results, without the depth required for a full-length research manuscript; (b) brief technical observation or advice; or (c) potential opportunities or avenues for further investigation, including a feasibility study.
- A Research Letter can report either descriptive or comparative data but the data analyses are not expected to be complex and are ideally preliminary in nature.
- For the simple or preliminary message to be conveyed in a Research Letter, it is expected that no statistics, or at most simple inferential statistics will be used. The more complex or advanced the statistical methods being used (e.g., those that might require specialist statistical review such as large association studies or network meta-analyses), the less likely the manuscript will be considered suitable as a Research Letter.
- A Research Letter in general is divided into the following sections: Introduction, Methods, Results, and Discussion.
- A Research Letter does not include an Abstract or Key Points.
- The text of a Research Letter contains up to **1,000 words** (not counting the title, authors, references) and up to **10 references**, with a maximum of **1 table and 1 figure**.
- The purpose of a **figure** is to illustrate the key point being made, so it is desirable only one figure is submitted. The figure may have up to four panels, but given the expectation of simple data presentation, the panels should not be overly detailed or complicated, and the need for more than a single panel figure must be self-evident. The greater the number of panels in a **figure** and the greater their complexity, the less likely the manuscript is suitable as a Research Letter.
- A Research Letter can have no more than **6 listed authors**. Other persons may be listed as collaborators in an online supplement: see authorship criteria below.
- It is possible that the peer review process will recommend that an article initially submitted as an Original Research Report is potentially acceptable as a Research Letter, especially where reviewers discern a simple message can be conveyed optimally in this abbreviated format.
- Online supplementary material is only allowed for brief additional and absolutely necessary methods but not for any additional results or discussion. Illustrative short video files are permitted as online supplemental material (but these should not be designed to serve the purpose of a Video in Clinical Anesthesia – see above). These online supplemental materials are numbered and cited consecutively in the text.
- A Research Letter otherwise should follow all of the guidelines for manuscript preparation and submission requirements and undergoes standard Journal peer review; all Journal policies stated herein apply to a Research Letter.
- Authors of a Research Letter should specifically review, and if applicable, state in the first sentence of Methods, adherence to Section 8.C. below on **Protection of Human Subjects**.
- A Research Letter cannot duplicate other material published or submitted for publication elsewhere.
- A Research Letter is published in the print and online editions of *Anesthesia & Analgesia*. A Research Letter is indexed in PubMed and is thus searchable and citable.

- Further resources:
  - Instructions for Manuscript preparation
  - Instructions for Figure preparation
  - Instructions for Table preparation
  - Instructions for Supplemental Material

Letter to the Editor (Back to Top)

- A **Letter to the Editor** is intended to offer brief, objective, and constructive comments or criticism. It may concern a previously published article or provide other short communication of general interest to the readership.
- A **Letter to the Editor** may be used to communicate results of studies that do not justify an Original Research Report or a Research Letter.
- This correspondence submission should not be a venue for a Case Report, although occasionally, a general reference to experience involving patient case material may be inherent in the text of the **Letter to the Editor**. If patient case material is included, authors of the Letter to the Editor should specifically review and state adherence to Section 8.C. below on **Protection of Human Subjects**.
- A Letter to the Editor can have no more than **4 listed authors**. No additional collaborators are permitted, but individuals may be listed in acknowledgements.
- A Letter to the Editor should be brief, with no more than **1000 words**, up to **6 references**, and **1 small table or pertinent illustration**.
- All Letters to the Editor should be submitted via the *Anesthesia & Analgesia* Online Submission and Review System, and not via email or postal service.
- A Letter to the Editor may be edited by the Correspondence Editor, sometimes extensively, to sharpen its focus. At the discretion of the Correspondence Editor, a Letter to the Editor may be sent for peer review. Separately, it will be sent to authors of the original article to which it refers for a response or rebuttal.
- A Letter to the Editor that is written in response to a published paper must be submitted no later than 3 months after the first of day of the month of the original article **print publication date**.
- Instructions for Manuscript preparation

Video in Clinical Anesthesia (Back to Top)

- A **Video in Clinical Anesthesia** is a unique platform for scholars to share instructional videos that have undergone the same rigorous peer-review process as other publications in the Journal.
- **This is the only article type that requires prior approval before submission (see below) and is not encompassed by the Journal "open format" policy. Before starting their video creation process, potential authors are requested to reach out to the *Anesthesia & Analgesia* Editorial Office to express their interest and to receive initial feedback from the Journal Editorial Board.**
- A **Video in Clinical Anesthesia** submission is accompanied by an appropriately rigorous and referenced manuscript.
- A Video in Clinical Anesthesia can have no more than **6 listed authors**. No additional collaborators are permitted, but individuals may be listed in the acknowledgements.
- The manuscript accompanying a Video in Clinical Anesthesia includes a Title Page but not an Abstract.
- The manuscript accompanying a Video in Clinical Anesthesia contains up to **2,000 words** (not counting the references), **10 references**, and **3 tables and/or figures**.
- A Video in Clinical Anesthesia otherwise should follow all of the requirements for manuscript and video content preparation and submission; all Journal policies stated herein apply to a Video in Clinical Anesthesia.
- Authors of a Video in Clinical Anesthesia should specifically review, and if applicable, state in the first sentence of Methods, adherence to Section 8.C. below on **Protection of Human Subjects**.
- A Video in Clinical Anesthesia should be no longer than 10 minutes in duration and cannot duplicate other material published or submitted for publication elsewhere.
- A Video in Clinical Anesthesia and its accompanying manuscript are published in the print and online editions of *Anesthesia & Analgesia*. A Video in Clinical Anesthesia is indexed in PubMed and is thus searchable and citable.
- All these videos will be published in both English and Spanish; the Editorial Office of *Anesthesia & Analgesia* can assist in the translation and production of these videos in Spanish.
- Further resources:
  - Instructions for Manuscript preparation
  - Instructions for Figure preparation
  - Instructions for Table preparation
  - Instructions for Supplemental Material

The Human Experience (Back to Top)

- **The Human Experience** is focused on the medical humanities. The content of The Human Experience encompasses literature, art, music, creative writing, philosophy, ethics, anthropology, ethnography, and history.
- These contributions to the Journal will focus on the first-hand accounts and personal perspectives of health care providers worldwide.
- Submissions to The Human Experience are intended to be brief vignettes.
- Specifically, either a short piece of original creative work (fiction or non-fiction prose, poetry, or annotated photography, digital image, music) **or** a very brief commentary on an existing work of art (painting, sculpture, folk/ethnic art, photograph, digital image, music)
- A Human Experience article can have no more than **4 listed authors**. No additional collaborators are permitted, but individuals may be listed in acknowledgements. Submissions to The Human Experience include a Title Page but not an Abstract.
- The Human Experience piece contains no more than 750 words and can have up to 3 illustrations.
- Audio or audiovisual material can be submitted as Supplemental Digital Content, with an absolute maximum file size of 100 MB.
- Individuals submitting an original creative work for The Human Experience can maintain its copyright and ownership.
- An included illustration can be a reproduction of a previously created work with the required appropriate attribution **and** written permission of its current copyright holder and/or current owner.
- Further resources:
  - Instructions for Manuscript preparation

- Instructions for Figure preparation
- Instructions for Table preparation
- Instructions for Supplemental Material

Synopsis of Eponymous Lecture

- Journal affiliate societies are welcome to encourage their annual eponymous lecture speaker, if they have one, to submit a synopsis of their lecture to the Journal. The submission process is as follows:
  - Each Journal affiliate society may only recommend one article per year, even if they have several annual eponymous lectures.
  - The affiliate society should contact the Journal Editor-in-Chief in advance, with the name of the speaker and the proposed title. Any initial agreement to proceed is not a guarantee of publication as the article will be peer reviewed.
  - The article should be submitted using The Open Mind article type and format with due attention to word count and reference limits.
  - The article title should be structured: "words that indicate what the lecture is about: eponymous title with year presented, affiliate society name" – for example (hypothetical), Improved Airway Management: Maplethorpe Lecture 2024, World Airway Society.
  - The content needs to be predominantly scientific, informative, topical, and forward-looking: for example, making recommendations for future directions in research or predicting future clinical developments.
  - A simple historical overview of the field is unlikely to be published.
  - In contrast, a useful guide to its content is to consider the following questions: How has the field evolved? What were the key scientific milestones? What insights can I as the lecturer provide to this development? For example, akin to a SWOT analysis: What mistakes were made? How could things have been done better? What was especially important or valuable? What work now needs to be done? Which developments are now anticipated?
  - Many eponymous lectures are understandably occasions for a highly personal, or (auto)-biographical celebration of the individual eminent lecturer. However, again, these are unlikely to be published – although, of course, (auto)-biographical elements will always appear within such an article.
- This guide is not comprehensive and should not be viewed as constraining style.
- Authors should expect their submission to undergo extensive line editing, after peer review, to optimize its readability.
- Instructions for Manuscript preparation

Endnotes

Pro-Con Debate papers published in *Anesthesia & Analgesia* are typically solicited by the Journal. These invited authors will follow these specific Pro-Con Debate manuscript instructions: Pro-Con Debate supplement.

Authors who are considering submitting an unsolicited **Pro-Con Debate** manuscript to *Anesthesia & Analgesia* should first contact the Journal Editorial Office at editor@anesthesia-analgesia.org, providing the proposed Pro-Con Debate topic and title, basic content outline, and author groups for both sides of the debate: all proposed authors should have agreed to participate. This initial inquiry will be reviewed by the respective Journal Section Editor. If approved to proceed with submission, authors will follow these specific Pro-Con Debate manuscript instructions: Pro-Con Debate supplement.

Several terms are used to describe a published **Clinical Practice Recommendation**: clinical practice guideline; consensus statement; position statement; practice advisory; and practice alert. *Anesthesia & Analgesia* (A&A) welcomes these types of papers. Authors will follow these specific Clinical Practice Recommendation manuscript instructions: A&A Clinical Practice Recommendation supplement.

The Journal does not accept **Research Methodology** articles [papers that discuss the research methods of a study alone].

SECTION 2: ARTICLE TYPES AT A GLANCE (Back to Contents)

Particular attention should be paid to the listed word count, reference count, and table/figure limits for each article type, both for an initial submission and any subsequent revisions.

These listed limits for word count, reference count, and tables/figures will be strictly enforced, resulting in a manuscript being returned to the author(s) for revision prior to any initial or a subsequent peer-review.

Please note, authors should mask patients' faces and remove patients' names from any figures, videos, or supplemental material containing images of patients unless they obtain written consent from the patients and submit written consent with the manuscript. Please note that it is not sufficient to mask patients' eyes.

***Anesthesia & Analgesia* - ARTICLE TYPES AT A GLANCE**								
Manuscript Type	**Abstract:**	**Author Count Limit**	**Figures/ Tables Limit**	**Reference Count Limit**	**Word Count Limit**	**Sections**	**Supplemental Material**	**Additional Information**
Clinical, Health Services, or Education Report	Structured 400-word limit & Key Points Summary	12	Up to 6 tables and/or figures	40	Up to 4000 (not including abstract and references)	Introduction, Methods, Results, and Discussion	When appropriate	EQUATOR checklist
Laboratory Research Report	Structured 400-word limit & Key Points Summary	12	Up to 6 tables and/or figures	40	Up to 4000 (not including abstract and references)	Introduction, Methods, Results, and Discussion	When appropriate	EQUATOR checklist ARRIVE checklist

Narrative Review Articles	Unstructured 400-word limit	12	Up to 6 tables and/or figures	100	Up to 5,000 words (not including abstract and references)		The inclusion of programing code/illustrative datasets as online supplemental material is encouraged	EQUATOR checklist
Systematic Review Article	Unstructured 400-word limit	12	Up to 6 tables and/or figures	100	Up to 5,000 words (not including abstract and references)		When appropriate	EQUATOR checklist
Meta-Analysis	Structured 400-word limit& Key Points Summary	12	Up to 6 tables and/or figure	150	Up to 5,000 words (not including abstract and references)		When appropriate	EQUATOR checklist
Editorial ***Solicited by the Editorial Board***	NA	4	1 table and/or 1 figure	20	Up to 3000 words (not including references)		When appropriate	EQUATOR checklist
The Open Mind	NA	4	Up to 3 tables and/or figures	20	Up to 3000 words (not including references)		When appropriate	EQUATOR checklist
Special Article	Unstructured 400 words	12	Up to 6 tables and/or figures	50-100 (See article description above for details)	Up to 5000 (not including abstract and reference)		When appropriate	EQUATOR checklist
Video in Clinical Anesthesia	NA	6	Up to 3 tables and/or figures	10	Up to 2000			EQUATOR checklist
The H… Expe…		4	Up to 3 illustrations	NA	Up to 750		When appropriate	EQUATOR checklist
Research Letter	NA	6	1 table and 1 figure	10	Up to 1,000	Introduction, Methods, Results, and Discussion, if applicable	When appropriate	EQUATOR checklist
Letter to the Editor and Reply – for *Anesthesia & Analgesia*	NA	4	1 small table or a pertinent illustration may be provided	6	Up to 1000			EQUATOR checklist
Synopsis of Eponymous Lecture	NA	4	Up to 3 tables and/or figures	20	Up to 3000 words (not including references)		When appropriate	EQUATOR checklist

Go to page 5

SECTION 3: STANDARDIZED STUDY REPORTING REQUIREMENTS (Back to Contents)

A. Enhancing the Quality of and Transparency of Health Research (EQUATOR) Network

The Enhancing the Quality of and Transparency of Health Research (EQUATOR) Network was created to monitor and to propagate the proper use of guidelines to improve the quality of scientific publications by promoting transparent and accurate reporting of human subjects, health services, and animal research.

As advocated by the EQUATOR Network, *Anesthesia & Analgesia* strongly encourages adherence to the applicable statement/guidelines and checklist for all submitted research-related manuscripts (see Table below). Manuscripts adhering to the applicable statement/guidelines and checklist will typically receive a more favorable review by the Journal.

Adhering to the applicable statement/guidelines and checklist promotes consistent study design and manuscript content, which are major advantages for the Journal's authors, reviewers, editors, and readers.

Authors should consult the EQUATOR Network webpage and/or the webpage URL or citation listed in the Table below for the most current version of the specific, applicable **statement or guideline and its checklist**.

- The applicable study checklist should be completed and uploaded under the EQUATOR Checklist File category at the time of initial manuscript submission via Editorial Manager.

Acronym	Full Title of Guideline	Webpage URL or Citation
CONSORT	Consolidated Standards of Reporting Trials (See footnote* below)	http://www.consort-statement.org/
TREND	Transparent Reporting of Evaluations with Nonrandomized Designs	http://www.cdc.gov/trendstatement/
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology	http://www.strobe-statement.org/
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses	http://www.prisma-statement.org/
SQUIRE	Standards for Quality Improvement Reporting Excellence	http://www.squire-statement.org/
SRQR or COREG	Standards for Reporting Qualitative Research Consolidated Criteria for Reporting Qualitative Research	PMID: 24979285 PMID: 17872937
CHEERS	Consolidated Health Economic Evaluation Reporting Standards	http://www.ispor.org/Health-Economic-Evaluation-Publication-CHEERS-Guidelines.asp
STARD or TRIPOD	Standards for Accurate Reporting of Diagnostic Tests *Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis*	http://www.stard-statement.org/ http://www.tripod-statement.org/
STREGA	Strengthening the Reporting of Genetic Associations	http://www.equator-network.org/reporting-guidelines/strobe-strega/
ARRIVE	Animal Research: Reporting of *In Vivo* Experiments	http://www.nc3rs.org.uk/arrive-guidelines

* The main CONSORT Statement is based on the "standard" two-group parallel design. However, there are several different types of randomized trials, some of which have different designs (e.g., cluster, non-inferiority and equivalence, or pragmatic trials), interventions (e.g., herbal medicinal, non-pharmacological, or acupuncture) and data (e.g., harms), for which specific CONSORT Extensions exist.

B. SPECIFIC STUDY TYPE AND ASSOCIATED PUBLISHED GUIDELINE

1. Randomized Controlled Trials. Authors reporting the results of a **randomized controlled trial** must follow the CONSORT statement and provide a completed CONSORT checklist. Authors must also provide a CONSORT flow diagram as Figure 1 of the submitted manuscript.

Please note that there are CONSORT Extensions for several different types of randomized trials, and the most applicable Extension should be followed by authors.

2. Non-Randomized Controlled Trials. Authors reporting the results of a **non-randomized controlled trial** must follow the TREND statement and provide a completed TREND checklist.

3. Observational Studies. Authors reporting the results of a **cohort, case-cohort, nested case-control, case-control, or cross-sectional study (or any other type of observational study of human subjects)**, or a retrospective data collection study must follow the STROBE statement and provide a completed STROBE checklist.

Authors submitting the results of such a quantitative observational study should clearly indicate (a) whether the primary outcome(s) were defined and established *a priori* at initiation of the study design or were created post hoc during data exploration ("data mining") and accompanying statistical analysis and (b) whether subgroup or sensitivity analyses were identified and established *a priori* or *post hoc*. For studies evaluating a treatment effect, indicate whether and how a clinically meaningful effect size was defined, once again either *a priori* or *post hoc*.

For further insights and directions, see Eisenach JC, Kheterpal S, Houle TT. Reporting of Observational Research in ANESTHESIOLOGY: The Importance of the Analysis Plan. Anesthesiology. 2016;124(5):998-1000.

4. Systematic Review or Meta-analysis. Authors reporting a **systematic review** or **meta-analysis of randomized trials or cohort studies** must follow the PRISMA (previously named QUOROM) Statement and provide a completed PRISMA checklist. Authors must also submit a PRISMA flow diagram as Figure 1 of the submitted manuscript.

5. Quality Improvement Research. Authors reporting the results of a **quality improvement study** must follow the SQUIRE 2.0 guidelines and provide a completed SQUIRE 2.0 checklist.

6. Qualitative Research. Authors reporting the results of a **qualitative study** (e.g., in-depth interviews and focus groups) must provide a completed SRQR checklist.

Alternatively, authors reporting the results of a **qualitative study** can provide a completed COREG checklist.

7. Mixed Methods Research. No definitive guidelines have been created for mixed (qualitative/quantitative) research. However, authors reporting the results of a mixed methods research study can reference the Good Reporting of A Mixed Methods Study (GRAMMS) framework.

See the following pertinent references:

Cameron RA, Trudy D, Scott R, Ezaz A, Aswini S. Lessons from the field: Applying the Good Reporting of A Mixed Methods Study (GRAMMS) framework'. Electronic Journal of Business Research Methods. 2013. https://works.bepress.com/roslyn_cameron/131/

O'Cathain A, Murphy E, Nicholl J. The quality of mixed methods studies in health services research. J Health Serv Res Policy. 2008;13(2):92-98.

O'Cathain A, Murphy E, Nicholl J. Three techniques for integrating data in mixed methods studies. BMJ. 2010 Sep 17;341:c4587.

8. Health Economic Evaluation Research. Authors reporting the results of a **health economic evaluation research study** must follow the CHEERS guidelines and provide a completed CHEERS checklist.

9. Diagnostic Accuracy. Authors reporting a **study of the accuracy of a diagnostic test** must follow the STARD statement and provide a completed STARD checklist. Authors must also provide a STARD flow diagram as Figure 1 of the submitted manuscript.

Alternatively, authors reporting studies of the accuracy of diagnostic tests can follow the TRIPOD Statement and provide a completed TRIPOD checklist.

10. Genetic Association Studies. Authors reporting a **genetic association study** must follow the STREGA guidelines and must submit a completed STREGA checklist.

11. Animal Studies. Authors reporting an **animal study** must follow the ARRIVE guidelines and must submit the ARRIVE checklist.

SECTION 4: STANDARDS FOR STATISTICAL METHODS AND STATISTICAL REPORTING (Back to Contents)

The Journal encourages adherence to the Statistical Analyses and Methods as Promulgated by the Statistical Analyses and Methods in the Published Literature (SAMPL) Guidelines as advocated by the EQUATOR Network, *Anesthesia & Analgesia*

Please see Lang TA, Altman DG. Basic statistical reporting for articles published in biomedical journals: The "Statistical Analyses and Methods in the Published Literature" or "The SAMPL Guidelines." Handbook, European Association of Science Editors. 2013:23-6.

The SAMPL Guidelines can be accessed at http://www.equator-network.org/reporting-guidelines/sampl/.

For All Studies That Include Data Analysis and/or Estimation

Basic statistical methods and reporting that should be included in all quantitative manuscripts.

The items outlined below are commonly missing or deficient in submitted manuscripts, leading to a lengthier and less favorable statistical review.

Authors are thus strongly encouraged to proactively address all these issues.

Authors are encouraged to review the "Study Design and Statistical Methods Reporting Checklist" consistently used by the handling Section Editor and statistical reviewer in evaluating a data-containing manuscript.

Please note that each manuscript will be explicitly evaluated on each of these items during its statistical review.

1. Abstract clearly and accurately states the study objectives/hypotheses and clearly describes data analysis and study findings
2. The Results section of the Abstract contains the key, relevant data as well as (where appropriate) confidence intervals and p-values: do not report just the p-values or use broad descriptive language
3. Study objectives and/or hypotheses clearly stated in the Introduction
4. Study design is appropriate for the stated aims. A common oversight is in association studies: if the authors assessed the association between an exposure and outcome in an observational study, they should collect or obtain sufficient data on potential confounding variables.
5. Primary and secondary outcomes clearly identified and defined a priori. While it is acceptable to present findings not anticipated in the study design, these should be clearly identified as post hoc observations.
4. Statistical methods appropriate and clearly described in a way that can be repeated by the reader
5. Baseline comparisons (e.g., height, weight, etc.) for randomized trial assessed with standardized difference: do not report P-values
6. Assumptions of the statistical analyses (e.g., normal distribution) appropriately assessed
7. Type I error/multiple testing adequately addressed. Generally, for comparisons of multiple groups for continuous data, factorial analysis of variance, followed by post hoc testing is preferred over multiple testing alone (even if adjusted for multiple comparisons

such as Bonferroni correction) [see: Pandit JJ. The analysis of variance in anaesthetic research: statistics, biography and history. Anaesthesia. 2010 Dec;65(12):1212-20.]

8. Missing data, data exclusions and potential sampling bias appropriately described and handled
9. Sample size justified. Usually this is done by specifying the minimum clinically important difference (MCID) for the primary outcome as part of the sample size calculation. The interpretation of results reflects this pre-specified threshold.
10. Results section follows clearly from the study objectives and statistical methods. Primary and then secondary aims should be addressed in sequence, with clear differentiation. No new statistical methods should be introduced in the Results, when they have not been stated and described earlier in the Methods.
11. Study data and outcomes are presented consistently and accurately in Abstract, Body of Manuscript, and Tables/Figures
12. Tables and Figures clear and self-explanatory
13. Precision of numbers reported with appropriate decimal places: generally, report data to 3 significant figures (i.e., 3.24 or 32.4; not 32.43)
14. Treatment effect estimates and their variability are reported, not just P-values. For proportions, report 95% confidence intervals.
15. Confounding is carefully addressed for observational studies
16. Limitations of design and statistical methods clearly described
17. Conclusions and Interpretations justified by the design and results
    - Causation/association– use words connoting association for observational studies
    - State "non-significant" instead of "similar/equivalent"
    - Avoid claiming that a certain outcome variable was "higher" or "more frequent" in one group than the other if (a) there is no statistically significant difference or (b) a formal hypothesis test was not performed
    - Trend: do not state "trend" for non-significant findings
18. P-values appropriately reported with specific values, not simply as $p<0.05$ or $p>0.05$ (except in case of $P<0.001$ where many programs do not report exact values to less than this; in describing analysis of variance across several comparisons)
19. "Multivariable" instead of "multivariate" when there are multiple independent/predictor variables and a single dependent/outcome variable.
20. Statistics for basic science and animal/cellular studies may be reported differently from clinical trials which is the focus of the guidance above:
    a. Sample sizing: there is rarely a 'minimum clinically important difference' so methods used to justify sample sizes for clinical trials are not meaningful. Nevertheless, some justification is needed, which may be by reference to previous work in the literature, or using arguments that take into the account the expected variability in results.
    b. Basic science studies are often organized as a series of different experiments, sometimes using different methods and techniques, with one experiment reliant on the results of the previous. It is sometimes necessary and acceptable to describe the relevant statistical methods within the specific subsection, and offer a more generalized description in the main Methods.
    c. For reporting of dose-response curves or relationships of two or more variables, it is likely that analysis of variance, or comparisons of curve fits by non-linear regressions are more suitable than multiple testing of individual data points.

SECTION 5: DIGITAL COPYRIGHT TRANSFER AGREEMENT (Back to Contents)

An Electronic Copyright Transfer and Disclosure Questionnaire is completed by the corresponding author during submission.

Upon submission, the co-authors are emailed a hyperlink to verify their co-authorship and complete the electronic Copyright Transfer and Disclosure Form within Editorial Manager.

Questions About the Copyright Transfer and Disclosure Form?

Please contact our editorial office at editor@anesthesia-analgesia.org

SECTION 6: OPEN ACCESS OPTION FOR PUBLICATION (Back to Contents)

Authors of accepted peer-reviewed articles have the choice to pay a fee to allow perpetual unrestricted online access to their published article to readers globally, immediately upon publication. Please see the **Open Access page** for more details.

SECTION 7: *ANESTHESIA & ANALGESIA* MANUSCRIPT PREPARATION (Back to Contents)

Manuscript Organization (Back to Top)

ALL articles should be arranged in the following order.

1. Manuscript, as a single file, consisting of Title Page, Abstract (not required for all article types – see Articles At A Glance), Body Text, References. Page numbers should be included, line numbers should not be included.
2. Tables (each Table should be a separate .doc file or placed at the end of the manuscript file)
3. Figure Legends (placed consecutively, in numerical order, all on the same page)
4. Figures (each Figure should be uploaded as a separate file)
5. Appendices(each Appendix should be a separate file)

Title Page (Back to Top)

- Article Title
- First name, middle initial, and last name of each author, with their highest academic degree (M.D., Ph.D., *etc.*), and institutional affiliations.
- Name, mailing address, phone number, and e-mail address of the corresponding author.
- Disclosure of funding received for the work from National Institutes of Health (NIH), Wellcome Trust, Howard Hughes Medical Institute (HHMI), and all other financial support, including departmental or institutional funding. If no funding received, state Financial Disclosures: None
- Please list any conflicts of interest the authors have had within the 36 months of submission. If no conflicts, state Conflicts of interest: None
- Clinical trial number and registry URL, if applicable.
- List the word count of the Abstract, Introduction, and Discussion. Also list the overall word count for the entire body of text (excluding Abstract and References).
- Abbreviated Title (running head) that states the essence of the article (< 50 characters). This is not required for all article types (see above).
- List each author's individual contribution to the manuscript. For each author, please list the individual contribution using the following text: "Author Name: This author helped…"

Abstract (Back to Top)

Manuscript Type	Abstract Type	Number of words
Original Clinical Research Report	Structured	400
Original Laboratory Research Report	Structured	400
Narrative Review	Unstructured	400
Systematic Review	Unstructured	400
Meta-Analysis	Structured	400
Editorial	NA	NA
The Open Mind	NA	NA
Special Article	Unstructured	400
Letter to the Editor	NA	NA

- Structured abstracts should use the following sections: Background, Methods, Results and Conclusions.
- Please include the abstract in the main document file after the title page. You will also be prompted to include the abstract text during the submission process in Editorial Manager.

Key Points Summary (Back to Top)

For **Original Clinical/Laboratory Research Reports** and **Meta-Analyses**, a "Key Points" summary should be included directly underneath the structured abstract. The key points summary should describe the Question, Findings, and Meaning, each composed of one sentence. Please format the summary as three bullet points:

- Question: [One Sentence Text]
- Findings: [One Sentence Text]
- Meaning: [One Sentence Text]

Body (Back to Top)

The body of the manuscript should typically be divided into four parts (does not apply to all article types – See Article Types At A Glance):

- Textual material (body text, tables, figure legends etc.) should be submitted as a .doc or .docx word processing file
- 12-point Arial or Times New Roman font
- Introduction (new page). This should rarely exceed one page in length.
    - Should ideally contain only 4 to 5 short paragraphs: (1) significance, (2) background, (2) rationale, and (3) the study's aims or objectives and if applicable, (5) primary study hypothesis, and if appropriate, the secondary study hypothesis.
    - Avoid the temptation and frequent tendency to provide an extensive literature review in the Introduction.
- Methods (new page)
    - A statement that the study was approved by the appropriate IRB/Research Ethics Committee and written informed patient consent was obtained, or that the requirement for written informed consent was waived. (See section C Protection of Human Subjects).
    - If applicable, authors should include their clinical trial registration number, registry, principle investigator and date of registration. Authors are required to provide, via the Anesthesia & Analgesia Editorial Manager interface, the specific link (Uniform Resource Locator, URL) to their trial registration at ClinicalTrials.gov or other applicable, valid oversight entity at submission for an Original Clinical Research Report that contains patient data. (See below section E: "Registration of Clinical Trials")
    - A statement indicating the author has followed the appropriate EQUATOR guidelines should be included in the Methods section.
        - Example: "This manuscript adheres to the applicable CONSORT guidelines."
    - A subsection entitled "Statistical Analysis" should appear at the end of the Methods section when appropriate
- Results (new page)
- Discussion (new page). Focuses on the findings in the current work

Acknowledgements (Back to Top)

For acknowledgement of individuals or organizations, provide complete name, degrees, academic rank, department, institutional affiliation, city, state, and country. Add description of the contribution to the study.

References (Back to Top)

- *Anesthesia & Analgesia* follows the American Medical Association (AMA) citation style; Consult the AMA Manual of Style, 11th ed., Oxford University Press, 2020 (https://www.amamanualofstyle.com), for style.
- Number references (as superscripts) in the sequence they appear in the text.
- In text, tables, and legends, identify references with superscript Arabic numerals.
- If there are 6 or fewer authors/editors, list all 6; if there are more than 6, list the first 3 followed by "et al."
- Abbreviate names of journals according to the journals abbreviation list maintained by PubMed
  Manuscripts "In Press" – A "manuscript in press" is defined as an article that has been accepted for publication but has not yet been published by the accepting journal, in print or online and is being cited as basis for the study being described in the submitted manuscript. Please submit an electronic copy (Word, PDF) of any "In Press" manuscript that is cited in the reference list, labeled as "In Press, Reference # ___."
- Do not include in the references any published papers that have been formally retracted or have had a statement of concern issued by the Journal that originally published the paper. Authors are expected to confirm prior to their initial manuscript submission that none of their presently cited references have been subsequently formally retracted or have had a statement of concern issued by the Journal that originally published the paper. For articles published in journals indexed in MEDLINE, the International Committee of Medical Journal Editors (ICMJE) considers PubMed the authoritative source for information about retractions. Per the ICMJE, retracted articles can be identified by using the following search strategy in PubMed: e.g., for an author J. Smith, enter "Smith*J AND retracted publication[pt]".
- Do not include in the references non-peer reviewed papers that have been uploaded to a preprint server.
- During revision, please double-check and confirm that your reference list and in-text reference citations are correct and updated to match the revised version of your manuscript. All references must appear in your reference list (even if the reference is not yet published), and a corresponding reference citation must also be cited in your manuscript for every reference listed in the reference list. In-text reference citations must appear in chronological order upon first mention in the manuscript.

Tables (Back to Top)

- *Anesthesia & Analgesia* follows the American Medical Associate (AMA) table format.
- Tables should be uploaded as a separate Word file or presented in the main document word file, just after the references.
- Use a separate page for each table.
- Individual tables should not exceed two typed pages. If a table exceeds two typed pages, start a new table on the subsequent page.

- For any table that exceeds two typed pages and cannot be divided into a new table, the table should be submitted as a supplemental digital content file (see formatting requirements for Supplemental Digital Content files below).
- Double-space all table material.
- Do not submit tables as photographs or pasted images. Tables should be black and white only.
- Number the tables consecutively and cite them consecutively (on first instance) in the text.
- Do not create multi-part tables (e.g., Table 1A, Table 1B). Such tables should instead be cited as "Table 1," "Table 2," etc.
- Each table should have a brief title.
- Each column in a table should have a brief column header name.
- Use footnotes (not table titles or column headings) for explanatory matter and definitions of acronyms or abbreviations. Acronyms and abbreviations must be described with footnotes even if they are defined in the text or in other tables or figures.
- For footnotes within a table, use lower-case italicized letters in sequential alphabetical order.
- If you include a block of data, a table, or a figure from another source, whether published or unpublished, acknowledge the original source.

Appendices (Back to Top)

- Uploaded as a separate file or in the main document file at the end of the body of text.
- Each appendix must be cited within the text, in consecutive order.
- Appendix content counts towards the table and/or figure limits. If the inclusion of an appendix exceeds the table and/or figure limit for the respective article type, submit the appendix as a supplemental digital content file.

Figure Legends (Back to Top)

- Supply a legend for each figure.
- Group figure legends on a single page just after the references
- If a figure has multiple panels (e.g., left, right or A, B, C) please specify each panel in the legend.
- Repeat definitions of any acronyms or abbreviations used in the figure in its legend.

Figures (Back to Top)

- Figures should be uploaded as separate .tiff, .jpeg, .pdf or .pptx files. Figures will have to be uploaded at a resolution of 300dpi or higher at acceptance.
- Figures with multiple panels should be condensed into a single file for each figure (for example, Figure 1A through 1F should be in one file, Figures 2a through 2F should be in a second file, etc.). Each individual panel should be labeled with a capital letter.
- *Anesthesia & Analgesia* publishes in full color and encourage authors to use color to increase the clarity of figures.
- Standard colors should be used (black, red, green, blue, cyan, magenta, orange, and gray).
- Avoid colors that are difficult to see on the printed page (e.g., yellow) or are visually distracting (e.g., pink).
- Figure backgrounds and plot areas should be white, not grey.
- Axis lines and ticks should be black and thick enough to clearly frame the image.
- Axis labels should be large enough to be easily readable and printed in black.
- Number figures consecutively. Supply a brief title for each. Cite figures in the text in consecutive, numerical order on first instance.
- If a figure has already been published, acknowledge the original source. You must obtain and submit written permission from the copyright holder to reproduce the material when you submit the manuscript for review. Unpublished figures require permission of the author. Permission is required to reproduce any previously published material except for documents or figures in the public domain. See Permissions
- Authors should mask patients' faces and remove patients' names from figures unless they obtain written consent from the patients and submit written consent with the manuscript. Please note that it is not sufficient to mask patients' eyes.
- Define in a footnote all acronyms or abbreviations used in each figure.

Visual Abstracts (Back to Top)

- Visual Abstracts can be created for an accepted article in one of three scenarios.

  1. At the discretion of Editor-in-Chief or the Section Editor handling the manuscript, the Journal can elect to produce a Visual Abstract for an article upon its acceptance, if it is concluded the Visual Abstract will benefit the article, its message, and intended audience.

  2. The author(s) can elect to purchase a Visual Abstract for their accepted article from Editage, the Journal preferred vendor. The Editorial Office will provide authors with details on contacting Editage at the time of manuscript acceptance.

  3. The author(s) can elect to create a Visual Abstract themselves. If authors elect to do so, they should use the A&A Visual Abstract Template. Authors should not submit a self-created Visual Abstract with their initial manuscript submission (so-called R0). Instead, authors should wait until their first manuscript revision (so-called R1) to submit their proposed self-created Visual Abstract.

Video preparation (Back to Top)

Note that the video preparation instructions here are for those accompanying original or other articles: for a Video in Clinical Anesthesia, see the instructions in the section above. The video clip(s) accompanying A&A submissions should conform to the following:

- Formatted in MPEG, QuickTime (MOV), Windows Media Video (WMV) or MP4.
- Play on *both* Windows and Macintosh platforms. The review process will be delayed if the Editorial Office cannot play your video clip.
- Individual size should not exceed 15 MB. Use video-compression software to reduce video size if necessary.
- Optimal video frame dimensions of 480 x 360 pixels and 640 x 480 pixels. Videos of 320 x 240 pixels have inadequate resolution for teaching.

- Duration of individual video clip should be less than 15-25 seconds.
- Combinations of clips: If you combine several video clips, for example several TEE echocardiographic loops, please provide adequate time for each segment, and leave a suitable gap between the videos. Use appropriate labeling to ensure that the viewer can understand the timing of the pathology and events. Labeling can be added with video editing programs such as Adobe Premiere or iMovie.
- Authors should mask patients' faces and remove patients' names from videos unless they obtain written consent from the patients and submit written consent with the manuscript. Please note that it is not sufficient to mask patients' eyes.
- Authors should complete a video checklist form for each video when submitting a revised manuscript. The video checklist form provides the information necessary to upload the video on the journal website's video gallery.

Supplemental Material (Back to Top)

- Authors may submit separate supplemental material to enhance their article's text and to be considered for online-only posting.
- Supplemental material may include the following types of content: text documents, graphs, tables, figures, audio, and video.
- Cite all supplemental digital content consecutively in the text (i.e., each supplemental file is numbered starting with 1)
- Citations should include the type of material submitted, should be clearly labeled, and should include a sequential number (Example "Supplemental Figure1", "Supplemental Table 1", "Supplemental Video 1").
- Supplemental Legends should be submitted at the end of the manuscript file and should provide a brief description of the supplemental content. For example: "Supplemental Table 1: Lists all medications used in this study."
- Each supplemental digital content file must be composed to standalone. For example, tables and figures must include titles, legends, and/or footnotes, following journal style, so the viewer can fully understand the supplemental content on its own. Production will not make any edits to the supplemental files; they will be presented as submitted.
- It is recommended to group multiple supplemental figures/tables into one supplemental digital content file when submitting. Each file will be given a permanent hyperlink when the Publisher prepares the supplemental digital content for posting. To avoid excessive hyperlinks in your publication, please group figures/tables.
- For audio and video files, enter the author name, videographer, participants, length (minutes), and size (MB) of file in Editorial Manager. Authors should mask patients' faces and remove patients' names from supplemental digital content unless they obtain written consent from the patients and submit written consent with the manuscript. Please note that it is not sufficient to mask patients' eyes. Copyright for video or audio supplemental digital content will be required upon acceptance.
- For a list of acceptable file types and size limits, please review LWW's requirements for submitting supplemental digital content: http://links.lww.com/A142

Additional Information (Back to Top)

1. Units of Measurement
   Use metric units. The units for pressures are mmHg or cmH2O. Diagonal slashes are acceptable for simple units, *e.g.*, mg/kg; when more than two items are present, negative exponents should be used, *i.e.*, ml · kg^{-1} · min^{-1} instead of ml/kg/min.

2. Drug Names and Equipment
   Use generic names. If a brand name must be used, insert it in parentheses after the generic name. Provide manufacturer's name, city, state, and country. Be careful about the use of trademarked terms (*e.g.*, Thrombelastography™, TEG™, *etc.*).

3. Statistical Analysis
   Detailed statistical methodology must be reported. Describe randomization procedures and the specific tests used to examine each part of the results; do not simply list a series of tests. Care should be taken with respect to a) parametric vs. nonparametric data, b) corrections for multiple comparisons, and c) rounding errors (summary statistics should not contain more significant digits than the original data). Median range (or percentiles) is preferred for nonparametric data.

4. Patient Identification
   Do not use patients' names, initials, or hospital numbers. An individual (other than an author) must not be recognizable in photographs unless written consent of the subject has been obtained and is provided at the time of submission.

Permissions (Back to Top)

At the time of their initial manuscript submission, authors must provide written permission from the copyright owner (usually the publisher) to use tables, or illustrations that have appeared in copyright form elsewhere, along with complete details about the source. Any permission fees that might be required by the copyright owner are the responsibility of the authors requesting use of the borrowed material, not the responsibility of Wolters Kluwer or the editorial office.

Verbatim quotations of copyrighted text material must be designated with quotation marks and have a cited attribution. Such direct quotations are appropriate when the content of the quoted text is novel and salient (e.g., a novel definition or unique description), and paraphrasing of it is thus not appropriate. Large amounts of routine text should not be reproduced and quoted verbatim in the manuscript.

To request permission and/or rights to use content from *Anesthesia & Analgesia*, access the Copyright Clearance Center) and enter *Anesthesia & Analgesia* in the 'Get Permissions' field in the upper-right corner. Please note: Permission will not be granted to adapt figures that have been previously published in *Anesthesia & Analgesia*. Contact the Editorial Office at editor@anesthesia-analgesia.orgfor further information.

Language Editing Services (Back to Top)

Articles submitted to the Journal must be written with a solid basis of English language. Awkward or non-intelligible English grammar and syntax can adversely affect the review process and the likelihood of acceptance of a manuscript. **Authors whose native language is not English should thus strongly consider having their manuscript copy-edited by a native English language medical/technical writer prior to initial submission.**

If you need assistance in preparing a manuscript for submission, our publisher, Wolters Kluwer, in partnership with Editage, offers a range of editorial services for a fee, including:

- Premium Editing: Intensive language and structural editing of academic papers to improve the clarity and impact of your manuscript.
- Advanced Editing: A complete language, grammar, and terminology check to give you a publication-ready manuscript.
- Translation with Editing: Write your paper in your native language and Wolters Kluwer Author Services will translate it into English, as well as edit it to ensure that it meets international publication standards.
- Plagiarism Check: Helps ensure that your manuscript contains no instances of unintentional plagiarism.
- Artwork Preparation: Save precious time and effort by ensuring that your artwork is viewed favorably by the journal without you having to incur the additional cost of purchasing special graphics software.

For more information regarding Wolters Kluwer Author Services and to receive a quote for your manuscript, please visit wkauthorservices.editage.com. Please note that use of Wolters Kluwer Author Services is at the discretion and cost of the authors and does not in any way imply a guarantee, or even a likelihood, of acceptance of your manuscript in *Anesthesia & Analgesia*.

Posting of Manuscript on Preprint Server (Back to Top)

For any manuscript submitted to *Anesthesia & Analgesia*, which has been previously posted by the authors on a preprint server: an online repository that enables online posting of an early version of the paper, the authors are required (a) to declare this previous activity; (b) to submit all previous reviews and different posted versions of the manuscript; and (c) to commit to linking electronically the latest preprint version to the version of record (VOR) if accepted for publication by *Anesthesia & Analgesia*.

SECTION 8: EDITORIAL, ETHICAL AND LEGAL REQUIREMENTS (Back to Contents)

Anesthesia & Analgesia follows the International Committee of Medical Journal Editors (ICMJE) "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals".

All authors submitting a manuscript to *Anesthesia & Analgesia* are required to understand and to adhere to the material below.

A. Role of Authors and Contributors

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3. Final approval of the version to be published; AND
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Authors must state in the Methods section of their manuscript that registration of their clinical trial occurred prior to the start of the trial and any patient enrollment undertaken.

A number of registries have been approved by the International Committee of Medical Journal Editors (http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/), including http://www.clinicaltrials.gov (the most commonly used registry in the United States), http://isrctn.org, http://www.umin.ac.jp/ctr/index/htm, http://www.anzctr.org.au, and http://www.trialregister.nl. Submissions that have registered with the European Clinical Trials Database, EudraCT (https://eudract.ema.europa.eu/) meet this requirement.

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Section 2: Draft Article

Type of article (Original)

Title: Perioperative outcomes of paediatric congenital cardiac surgery in Johannesburg, South Africa

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Abstract

Background

Congenital cardiac diseases are the commonest congenital birth defects with children undergoing surgery at increased risk of mortality. Outcomes following congenital cardiac surgery in children has been well documented in high-income countries for many years, but little is known from the African continent.

Aim

The aim of this study was to determine factors associated with perioperative mortality in patients that underwent congenital cardiac surgery at our institution.

Methods

This retrospective cross-sectional study was conducted at Charlotte Maxeke Johannesburg Academic Hospital spanning a period of 12 years (2006-2017). The surgical, ICU, and anaesthetic records of patients that underwent surgery between 1 January 2006 and 31 December 2017 were reviewed. A multivariable regression analysis was performed for the factors which had a p-value of 0.1 and less in the univariable regression analysis. A Cox regression analysis was performed for mortality over time. All hypothesis testing accepted a p-value of <0·05 as statistically significant.

Results

There was an 11% (188/1701) in-hospital mortality rate overall. Patients that died were primarily younger, 0·33 years (IQR 0·13 - 1·25) vs 2·08 years (0·92 -5·33), had lower median weight of 5kg (IQR 3·45 – 8·20) vs 10·3kg (7·50 –17·7), longer cardiopulmonary bypass 179min (16·0 - 272·5) vs 112min (81·0 -152·0) and aortic cross clamp times 82·5min (35·0 -139·0) vs 65·0min (36·5 -98·0). Palliative surgeries had the highest mortality rate with 41% of all mortalities coming from this category. Cardiopulmonary bypass time ($p < 0·001$), ICU length of stay ($p < 0·001$), aortic cross clamp time ($p = 0·001$), days on the ventilator ($p < 0·001$), and the STAT 2020 mortality score ($p = 0·04$) were independently predictive of perioperative all-cause in-hospital mortality in a multivariable regression model. The model yielded an area under the curve of 90%. Of those that presented for surgery, approximately 43% were operated in same year as presentation.

Conclusions

Perioperative mortality following congenital cardiac surgery was higher in our study group compared to high income countries but it was similar to that of other low-middle income countries. Current predictive scoring systems were inconsistent in our study population with the STAT 2020 mortality score being predictive in a

multivariable regression analysis (p = 0·038) and the RACHS-2 score in a cox regression analysis (p = 0·002).

Wordcount: 348

Key words: mortality, congenital cardiac surgery, paediatric, Rachs-2, STAT 2020, ABC

Key points summary

Question: [What are the perioperative risk factors associated with mortality in pediatric patients undergoing congenital cardiac surgery in an upper-middle-income country with resource constraints?]

-Findings: [Overall mortality rate in this study is 11%. Cardiopulmonary bypass time, ICU length of stay, aortic cross clamp time, days on the ventilator, and the STAT 2020 mortality score were independently predictive of perioperative all-cause in-hospital mortality in a multivariable regression model.]

-Meaning: [There is an associated increased mortality not reflected by the conventional risk stratification scores. A contextual risk stratification strategy informing which patient would undergo surgery safely in this limited resource environment is necessary.]

Introduction

Congenital cardiac diseases are the most common congenital birth defects with a global incidence of four to eight cases per 1000 live births.[1] In South Africa, Hoosen et al. (2011)[2] reported an estimated prevalence of 0.6 to 0.8 cases per 1000 live births with approximately 11000 children born each year with congenital heart disease.[2] Approximately 40% of these children require surgical interventions each year [2,3].

There is a paucity of perioperative outcome data for paediatric and neonatal congenital cardiac surgery from the African continent and other lower- and middle income countries [4]. A large proportion of patients experience delayed referrals due to a lack of specialised centres to perform cardiac surgery, shortage of trained specialists, high cost and inadequate investment in health [1]. These issues exist in a number of low-to-middle income countries (LMICs) [1]. Reports show that only one to five percent of children requiring cardiac surgical intervention received care in LMICs [5 6].

With the developments and advances in paediatric cardiac surgical services, several studies have reported good outcomes in high income countries [7,8]. Perioperative mortality has been found to be associated with complexity of surgery and volume of

cases [9]. In the few studies published from upper middle-income countries (UMIC) like Brazil and China, higher morbidity and mortality were reported. [1,7] The current study is the first report detailing perioperative outcomes in a South African public healthcare centre.

High-income countries, primarily in North America and Europe, have large databases used to develop risk adjustment tools to risk stratify patients [10]. The risk stratification tools used include the Risk Adjustment for Congenital Heart Surgery (RACHS-1) [11] (updated to RACHS-2) [12], the Aristotle Basic Complexity (ABC) levels, and the Society of Thoracic Surgeons (STS)–European Association for Cardio-Thoracic Surgery (EACTS) Congenital Heart Surgery Mortality categories and scores (STS-EACTS Mortality Score and Categories, commonly referred to as "STAT Mortality Scores and Categories")[13] (updated to STAT 2020 scores and categories)[14]

We embarked on a 12-year single-centre retrospective study to determine the mortality rates and the factors associated with perioperative mortality of paediatric patients presenting for congenital cardiac surgery at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) in Johannesburg, South Africa.

Methods

Approval to conduct the study was obtained from the Human Research Ethics Committee (HREC) of the University of the Witwatersrand (Ethics clearance number M211151). Ethical principles as governed by the South African Guidelines for Good Clinical Practice [15] and the Declaration of Helsinki [16] were strictly followed. This was a retrospective cross-sectional study of all consecutive patients less than 18 years of age who underwent congenital cardiac surgery at CMJAH during a 12-year period (1 January 2006 to 31 December 2017). These dates were chosen as paediatric cardiac surgical services were terminated at the facility in 2017. Patient records were accessed via the electronic database of surgical, ICU and Anaesthetic records. Patients were excluded if records were incomplete (>50% of data was required for a record, otherwise it was excluded). Furthermore, if patients were older than 18 years of age or underwent cardiac surgery other than congenital cardiac surgery, they were also excluded (Figure1).

CMJAH is a 1088 bed quaternary hospital that serves the public sector. During the study period, CMJAH was one of only five major public centres in South Africa to offer comprehensive paediatric cardiac services [17]. This centre (CMJAH) had one

senior paediatric surgeon who worked for the most part of the study period, with two new surgeons joining the centre in the latter part of the study period. The current study intended to use all available records. However, a minimum adequate sample size was still calculated.

This minimum adequate sample size was calculated using a published equation recommended for determining the sample size required for developing a clinical prediction model, in this case both a binary outcome model such as a logistic regression and or a time to event model (Proportional hazard regression).[18]

Taking the number of candidate predictor parameters for potential inclusion in the new model as 10, and the expected Cox-Snell's adjusted R squared as 50%, with a desired shrinkage parameter of 90%, the sample size was calculated as 289. Supplementary Table 1 (Sample size computation parameters) demonstrates all the factors and criteria used to determine the sample. Importantly, the nature of the study allowed the researchers to use all the records that were available, which was a number significantly higher than the minimum required sample size.

Each available patient record was assigned a study number, and the relevant variables were recorded on Microsoft® Excel for Windows. All data were collected by one

author (PS) and a second reviewer (and originator of the database) assisted in minimising transcription error from the database to an excel spreadsheet. The following study definitions were used: paediatric patients – patients less than 18 years of age; in-hospital mortality – all-cause mortality that occurred during or after the completion of congenital cardiac surgery in-hospital within the same admission. Mechanical support included patients that required extracorporeal life support or ventricular assistive devices.

The collated data were analysed using Stata 16 [Stata Corp LP Statistics/Data Analysis Copyright 1985 – 2013 Stata Corp 4905 Lakeway Drive Special Edition College Station, Texas 77845 USA 800– STATA]. Categorical data were analysed using percentages and frequencies. Continuous variables were reported with the use of means (standard deviation) or medians (interquartile range) depending on distribution. Relationships between perioperative in-hospital mortality and variables such as patients' characteristics, and risk stratification scores (RACHS-2, ABC and STAT 2020) were compared using paired and unpaired Student's t-tests for parametric data, or Mann-Whitney and Wilcoxon matched pairs for nonparametric data. A multivariable regression analysis was performed for those variables of univariable regression analysis with a p-value ≤ 0·1. A Cox regression analysis was performed for mortality over time. A p-value of <0·05 was accepted as significant.

Results

A total of 1701 patients underwent congenital cardiac surgical procedures (Figure 1). The median age of patients was 1·92 years with a median weight of 10 kg at first recorded surgery (Table 1). A total of 2222 operations occurred with 521 of these being repeat operations (Table 1).

One hundred and eighty-eight (11%) patients died during the study period. Patients who died were predominantly younger (median age of 0·33 years), had lower median weight at the time of surgery related to mortality (5 kg), longer median cardiopulmonary bypass (179 min) and aortic cross clamp times (82·5 min). Fifty-eight (3.4%) patients required mechanical life support in the form of extracorporeal life support (ECMO). Of these, 42 (72·4%) died (refer to table 1).

Most repeat surgeries (Supplementary Figure 1) occurred amongst complex and palliative surgeries, followed by tetralogy of Fallot repair surgeries and ventricular septal defect repairs. Out of the 521 repeat surgeries, 415 were performed during the same hospital admission (early repeat) whilst 106 were performed at subsequent admissions (late repeat surgeries) within the study period. Patent ductus arteriosus

(PDA) ligations were the only procedures that involved one-time definitive repair and did not require repeat surgeries.

Palliative surgeries had the highest mortality rate of 77/188 (41%) followed by complex repairs 35(18·6%) and atrio-ventricular canal repair group 20 (10·6%) (Supplementary Figure 2). Yearly total mortality ranged from 4·7% to 11·4%, with variations existing in mortality rates from individual procedures per year (Figure 2). Mortality also varied between surgical category within a year (Figure 3).

A relationship between mortality and existing predictive scores/categories showed that there was significantly higher mortality with RACHS-2 score category 5, and STAT 2020 category 5 (Table 1). Survival was significantly higher in the RACHS-2 score categories 1, 2, and 4; ABC levels 1 and 4; and STAT 2020 categories 1,3 and 4 (Table 2). The following variables had a univariable association with mortality: younger age; lower weight; longer CPB time; longer aortic cross clamp time; longer ICU stay; longer ventilated days; STAT mortality score; ABC score; RACHS-2 categories 2, 3, 4 and 5; STAT 2020 mortality categories 2, 3, 4 and 5; and ABC complexity levels 2, 3 and 4 (Table 2).

Cardiopulmonary bypass time, ICU length of stay, aortic cross clamp time, days on the ventilator and the STAT 2020 mortality score were independently predictive of perioperative all-cause in-hospital mortality in a multivariable regression model. The RACHS-2 score, STAT 2020 mortality categories, and ABC scores and complexity level were not predictive of in-hospital all-cause mortality.

The multivariable regression model was highly predictive of mortality and yielded an area under the curve of 0.90 (Supplementary Figure 3). A total of 11 patients had an unspecified RACHS 2 score. In a Cox regression model, a unit increase in a RACHS-2 score was associated with a 60% increase in the risk of mortality (Table 3). Cardiopulmonary bypass time was also associated with mortality over time. Although longer CPB time was strongly associated with mortality, it did not have any influence on survival over time.

On average 246 patients with congenital cardiac lesions presented annually, and only 42·6 % were operated on that same year (Supplementary Table 2). Approximately 12% patients on average, were either refused surgery (due to inoperable lesions) or died preoperatively while 45.4% were not operated on by end of year of presentation- (Supplementary Figure 4).

Discussion

The main finding in this study was a perioperative mortality rate of 11%. Prolonged cardiopulmonary bypass time, ICU length of stay, aortic cross clamp time, days on the ventilator and the STAT 2020 mortality score were independently predictive of perioperative all-cause in-hospital mortality in a multivariable regression model. Extracorporeal life support in the form of ECMO or VAD was associated with less than 30% survival. The generated model had a high area under the curve, indicative of a highly predictive model.

Data from our centre shows mortality variability dependent on cardiac lesion complexity, with 0% amongst ASD surgery, and 41% in palliative repairs. The mortality also differed year on year with some years seeing higher mortality of these non-complex surgeries. The combination of PDA, VSD and AV canal had the highest fluctuation in mortality from 0 - 21%, which may have been related to personnel changes. The all-cause mortality rates of simple congenital heart diseases such as ASD, VSD and PDA were higher in our centre collectively compared to HIC including Europe and China (3·2% compared to 0·99% and 0·43% respectively)[19].

At its peak the paediatric cardiothoracic surgical compliment at our institution, was made up of one senior specialist with two junior specialists as evidenced in an audit by Hoosen et al (2010)[17]. Evidently this is far from the need documented by Hoosen et al (2017)[20]. More palliative and complex cases were also operated on during this period. Our data indicate that on average only 40% of patients requiring cardiac surgery are operated on in the year they presented, resulting in an annual accumulation of patients awaiting surgery. The local perioperative team had a low median volume of paediatric congenital heart disease cases with approximately 105 performed annually. In addition, the same team would operate/assist in procedures on paediatric and adult rheumatic heart disease and grown-up congenital disease (GUCH) patients.

Case volumes are described as low volume when <150 cases are performed, medium volume when 150-249 cases are performed per year and high volume when >250 are performed per year [21]. It has been shown that there is an inverse relationship between the number of congenital cardiac surgeries performed in a centre per year and mortality with centres that perform large volumes of cases attracting lower mortality rates [21,22]. However, this relationship has also been shown to be complex and multifactorial [21] Brown recommend that there be a differentiation between

comprehensive (greater than 200 index cases per year) and essential (a minimum of 75 index cases per year) pediatric cardiac centres.[23] The effect of low volume centres is magnified in rare high-risk procedures

Riley, Murphy and Mastropietro [24] found a variety of modifiable (preoperative mechanical ventilation and nutritional status, longer CPB, staffing) and non-modifiable factors (younger age, lower weight and increased surgical complexity) associated with cardiac arrest after paediatric cardiac surgery. Infants < 1yr with CHD have a lower body weight, require specialised skills, and have a higher risk of anaesthesia, resulting in the higher mortality [25]. This correlation was also observed by by Zheng et al [25] but was in contrast to the study performed by Sharifi et al (2023) [26] that showed no significant relationship between weight and age with mortality in their patient population.

Furthermore, the variables of surgical complexity and CPB duration are related, as typically more complicated surgeries require longer duration of bypass. Children with longer CPB times and complex surgical repairs, as seen in our palliative and complex population, should be viewed as very high risk and prone to postoperative complications. In-depth analysis and identification of these risk factors in our

population would allow for the institution of timely and effective strategies and management algorithms targeted at the vulnerable population.

The Global Burden of Disease and Injury Risk Factor (GBDIRF) study found a 4.2% global increase in birth prevalence of congenital cardiac disease (CCD) between 1990 and 2017. For a child who presents with CCD in the South African public sector, affordable comprehensive cardiac healthcare is restricted due to the limited number of centres that perform surgery in South Africa. Zilla et al (2018)[27] reported 46 (8 public and 38 private) centres while Roussouw[28] reported the decline to 22 centres in 2021. Limited staff training and retention strategies, and lack of administrative prioritisation of CCD has contributed in this decline.[28]

In an estimated population of one billion on the African continent, approximately 2 500 to 3 000 children undergo cardiac surgery annually [29]. South Africa and Egypt are said to have better cardiac services than most countries on the African continent [27]. However, deficiencies are still evident in these countries. There is low availability of services in the public sector, with South Africa said to be operating on only 40% of required for CHD [27]. It is also estimated that 50 public compared to 530 private cardiac patients per million were operated on in South Africa annually [27]. Higashi et al

[30] estimated that only 3% of children who needed surgery in Sub-Saharan Africa were operated on.

Mortality data for congenital cardiac surgery in LMIC and particularly in Africa, are under-reported. In high income countries (HIC), perioperative mortality rates (POMR) have reportedly decreased from 8·7% to less than 4% [9,31,32]. In a few of the LMIC where data is available, higher morbidity and mortality were reported, with Cavalcante et al [7] quoting a POMR of 11·6% [1,7]. This rate is similar to findings in our study.

Perioperative outcomes data in Africa are very few and skewed by complex cardiac surgery being performed by mission surgical camps or definitive surgical care taking place in countries outside of the continent [33,34]. This limits an assessment relating outcomes to local skill sets and resources. Kinsley et al [35] who established a successful private-public partnership through the Walter Sisulu Paediatric Cardiac Centre, documented the need for congenital cardiac surgery in Africa. Hoosen et al [20] audited paediatric cardiac services in South Africa and noted that there were deficiencies at multiple levels that contributed to the needs of children with CHD not being met.

In Northern Uganda, of the 224 patients that needed surgery, only 57 received definitive intervention, with a proportion of them being operated on in Germany, the Cayman Islands, and India through funding from charity organizations [36]. In Mozambique, Mocumbi et al [33] reported late presentations among their congenital cardiac patients where 29% presented with complications at time of diagnosis. Their operation rate was 36% with only 26% having complex lesions. In Rwanda, only 149 open cardiac procedures had been operated on over a 10 year period by the Team Heart, a humanitarian international effort [37]. This study is the first to provide insight into the perioperative mortality outcomes of paediatric congenital cardiac surgeries operated on in Africa by local surgeons in a public sector facility.

Given the extensive range of surgical procedures available to correct congenital heart diseases, comparison of mortality should follow a risk stratification system. Our study demonstrated that there was higher mortality with higher levels of the RACHS-2 score, and STAT 2020 categories. This finding contrasts with studies conducted in other middle-income countries and those in HIC [7,38,39] where the RACHS-1 score was predictive of mortality in their patient populations. The STAT 2020 scoring system now includes more procedure codes than its predecessor, which may contribute to the STAT score being predictive of mortality in our population.

There is a reported 90-95% survival to adulthood with good long-term outcomes due to advances in cardiac treatment modalities in recent decades [38,39]. These reported advances are still not available to over 90% of the children with CHD in LMICs. Despite mortality being historically used as a measure for evaluating quality of cardiac surgical services, its use to compare services in the paediatric population may not be suitable for surgical outcomes [21]. Mortality depends on a range of factors which in turn may have regional differences amongst high, middle- and low-income countries.

The limitation of the study is its retrospective single centre nature and thus may not be generalisable even to the South African population. South Africa is meant to have the best services in Africa alongside Egypt, with Johannesburg and Cape Town being the most resourced[27], but however, this is not the case. This discrepancy is evidenced in Hoosen et al. (2010)[17], with outcomes data not being reported. The time effect in this study might have resulted in a bias, in that events and outcomes of interest were time related. However, the bias is addressed by using medical reports of surgeries performed by a single cardiothoracic surgeon who is a co-author in this paper.

The cross-sectional nature of the study limits our ability to investigate causality of the covariates to morbidity and mortality. A second data reviewer (and the originator of the database) assisted in minimising transcription errors from paper-based database to Microsoft Excel spreadsheet. Further prospective studies will assist us to increase our understanding of the unique variables that may contribute to the higher mortality rates seen in our patient population and to assess morbidity.

Careful patient selection and medical optimization of patients aligned with specific expertise at dedicated children's hospitals may lead to improvement in mortality rate. Future studies comparing the outcomes of patients with cardiac disease based on hospital type, surgical volume as well as surgical skill may help determine the future of care including potential need for regionalization of pediatric cardiac centres for this vulnerable patient population.[19]

Conclusion

This is the first report looking at surgical outcomes after paediatric congenital cardiac surgeries performed at a centre in the South African by local personnel and not involving mission surgical camps within the African context. Delayed referral of children to specialised centres leads to presentation with a range of severe associated

comorbidities and complications such as renal dysfunction, pulmonary hypertension, systemic infection, poor nutritional status, un-attended genetic syndromes, and severe ventricular dysfunction.[40] These factors are likely not as commonly encountered in higher income countries from which the current risk stratification systems were created.

The cohorts of patient data sets used to develop these scoring systems are not representative of patients globally. This is an area that will require further research and analysis and may be used to define contributing factors for the higher mortality rates seen in our population. These data will hopefully pave the way to increase the understanding of the contributing elements to the higher mortality rates in our population and thus assist in improving the congenital cardiac surgical services in South Africa and other comparable middle-income nations.

Acknowledgments

The study had no external funding.

Declaration of interests

This research was partially conducted with the intention to fulfil a Master of Medicine degree. We declare no external funding or competing interests.

Supplements

Supplementary Appendix 1: Definitions of terms used (research assumptions) for this study.

Supplementary Figure 1. The distribution of repeat surgeries.

Supplementary Figure 2. Mortality outcomes per procedure.

Supplementary Figure 3. The ROC curve for the multivariable regression model.

Supplementary Table 1. Sample size computation criteria.

Supplementary Table 2. Total case presentation counts, and proportions operated on.

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Table 1. Sociodemographic factors, clinical parameters, risk stratification tools and the association with mortality

Parameter		Mean (SD)/Median (IQR)/n (%)			
		Overall (n = 1701)	**Mortality (n = 188)**	**No Mortality (n = 1513)**	**P value**
Age		1·92 (0·67 – 4·83)	0·33 (0·13 - 1·25)	2·08 (0·92 - 5·33)	<0·001
Weight		10·0 (7·00 – 16·0)	5·00 (3·45 – 8·20)	10·3 (7·50 – 17·7)	<0·001
Gender	**Males**	824 (48·4%)	79 (51·6%)	727 (48·1%)	0·69
	Females	858 (50·4%)	91 (48·4%)	767 (51·9%)	
Aortic Cross Clamp Time		65·0 (36·0 - 100·0)	82·5 (35·0 - 139·0)	65·0 (36·5 - 98·0)	0·01
CPB Time *		116·0 (82·0 - 159·0)	179 (16·0 - 272·5)	112 (81·0 - 152·0)	<0·001

LOS ICU †		5·0 (3·00 - 8·00)	8·0 (3·0 – 16·5)	4 (3·0 – 8·0)	<0·001
Ventilator Days		2·0 (1·0 – 5·0)	8·0 (3·0 – 16·0)	2·0 (1·0 – 4·0)	<0·001
Mechanical Life Support	**Yes**	58 (3·4%)	31(16.5%)	27 (1.8%)	<0·001
	No	1643 (96·7%)	157 (83·5%)	1486 (98·2%)	
RACHS-2					
1		494 (29·2%)	16 (3%)	478 (97%)	<0·001
2		901 (53·3%)	63 (7%)	838 (93%)	<0·001
3		46 (2·7%)	8 (17%)	38 (83%)	0·07
4		242 (14·3%)	64 (26 %)	178 (74%)	<0·001
5		6 (0·4%)	5 (83%)	1 (17%)	<0·001
ABC Complexity levels					
1		399 (23·5%)	14 (4%)	385 (96%)	<0·001
2		832 (49·0%)	78 (10%)	754 (90%)	0·98
3		380 (22·4%)	38 (10%)	342 (90%)	0·66
4		88 (5·2%)	28 (32%)	60 (68%)	<0·001
STAT 2020 Mortality Category					
1		727 (42·9%)	21 (3%)	706 (92%)	<0·001
2		644 (38·0%)	59 (9%)	585 (91%)	0·96

3	208 (12·3%)	50 (24%)	158 (76%)	<0·001
4	111 (6·5%)	23(21%)	88 (79%)	<0·001
5	6 (0·4%)	5(83%)	1 (17%)	<0·001

**CPB – cardiopulmonary bypass, † LOS– length of stay in days, ICU - intensive care unit*

Table 2. Regression Analysis Model for Mortality

Characteristic	N	Univariable		Multivariable	
		OR (95% CI)	p-value	AOR (95% CI)	p-value
Age	1701	0·69 (0·61, 0·77)	<0·001	0·83 (0·63, 1·05)	0·2
Weight (Kg)	1701	0·82 (0·78, 0·86)	<0·001	1·01 (0·90, 1·11)	>0·9
CPB time (in mins)	1197	1·01 (1·01, 1·01)	<0·001	1·02 (1·01, 1·02)	<0·001
ICU stay (in days)	1625	1·03 (1·02, 1·05)	<0·001	0·68 (0·57, 0·79)	<0·001
Aortic Cross Clamp time (mins)	1219	1·01 (1·00, 1·05)	<0·001	0·99 (0·98, 0·99)	0·001
Ventilated days postop	1533	1·06 (1·05, 1·08)	<0·001	1·54 (1·32, 1·84)	<0·001
STAT 2020 score	1701	8·33 (5·57, 12·5)	<0·001	24·6 (1·11, 512)	0·04
ABC Basic Score	1701	1·33 (1·23, 1·45)	<0·001	1·13 (0·68, 1·94)	0·7
Gender (n=1701)	**Female**	**Reference**		**Reference**	
	Male	1·04 (0·75, 1·44)	0·8		

RACHS-2 (n=1690)	**1**	**Reference**		**Reference**	
	2	2·32 (1·36, 4·2)	0·003	1·14 (0·35, 4·16)	0·8
	3	6·34 (2·44, 15·4)	<0·001	2·2 (0·36, 13)	0·4
	4	10·8 (6·22, 19·7)	<0·001	1·85 (0·25, 13·4)	0·5
	5	151 (22·6, 2977)	<0·001	0 (0·00, 6·72)	0·14
STAT 2020 Mortality Category (n=1701)	**1**	**Reference**		**Reference**	
	2	3·39 (2·07, 5·78)	<0·001	1·73 (0·63, 5·03)	0·3
	3	10·5 (6·24, 18·4)	<0·001	0·31 (0·04, 2·34)	0·3
	4	8·81 (4·68, 16·7)	<0·001	0·15 (0·01, 3·56)	0·2
	5	169 (25·8, 3307)	<0·001	N/A	N/A
ABC Complexity Level (n=1701)	**1**	**Reference**		**Reference**	
	2	2·86 (1·65, 5·33)	<0·001	0·66 (0·12, 4·56)	0·7
	3	3·07 (1·67, 5·96)	<0·001	0·68 (0·05, 11)	0·8
	4	12·9 (6·53, 26·6)	<0·001	0·33 (0·01, 11·8)	0·5

**OR = Odds Ratio, CI = Confidence Interval*

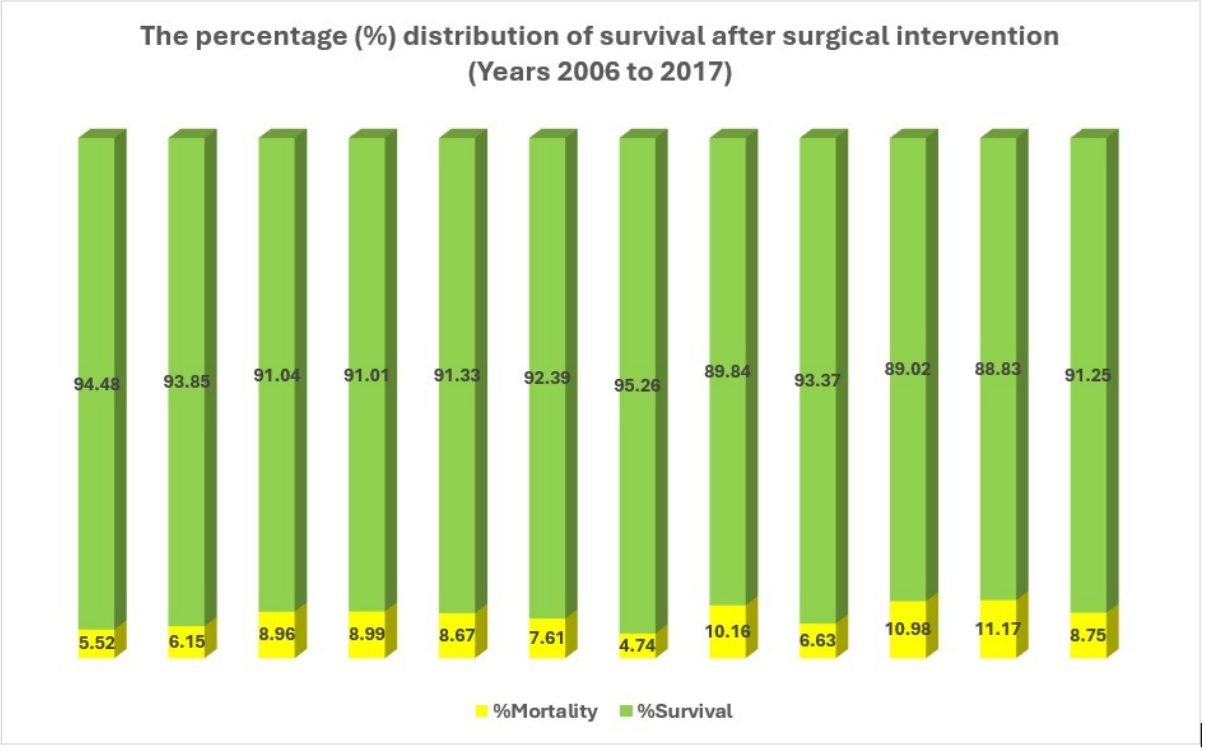
Table 3. Cox regression analysis of mortality

Parameter	HR	Std. Err.	Z	95%CI	P>|z|
Age	0·80	0·10	-1·82	0·63, 1·02	0·07
Weight (kg)	1·00	0·05	0·03	0·91, 1·11	0·98
ICU stay	0·97	0·03	-1·07	0·91, 1·03	0·28
Ventilated Days	1·02	0·04	0·47	0·95, 1·10	0·64
CPB time (min)	1·00	0·00	5·68	1·00, 1·01	<0·001
AoXCl time (min)	1·00	0·00	-0·53	0·99, 1·00	0·59
Gender	1·18	0·26	0·75	0·76, 1·83	0·45
RACHS-2	1·40	0·16	3·04	1·13, 1·75	0·002
ABC Complexity Level	0·91	0·16	-0·52	0·65, 1·29	0·61
STAT2020 Mortality category	1·30	0·42	0·82	0·69, 2·46	0·42

*HR = *Hazard Ratio, CI = Confidence Interval, AoXCl = aortic cross clamp*


TOTAL NUMBER OF RECORDS: 1968
Records included: 1701
Records excluded: 267
Reason for Exclusion
• 152 cases older than 18years,
• 115 were either premature or GUCH

Figure 1


The percentage (%) distribution of survival after surgical intervention
(Years 2006 to 2017)
94.48
93.85
91.04
91.01
91.33
92.39
95.26
89.84
93.37
89.02
88.83
91.25
5.52
6.15
8.96
8.99
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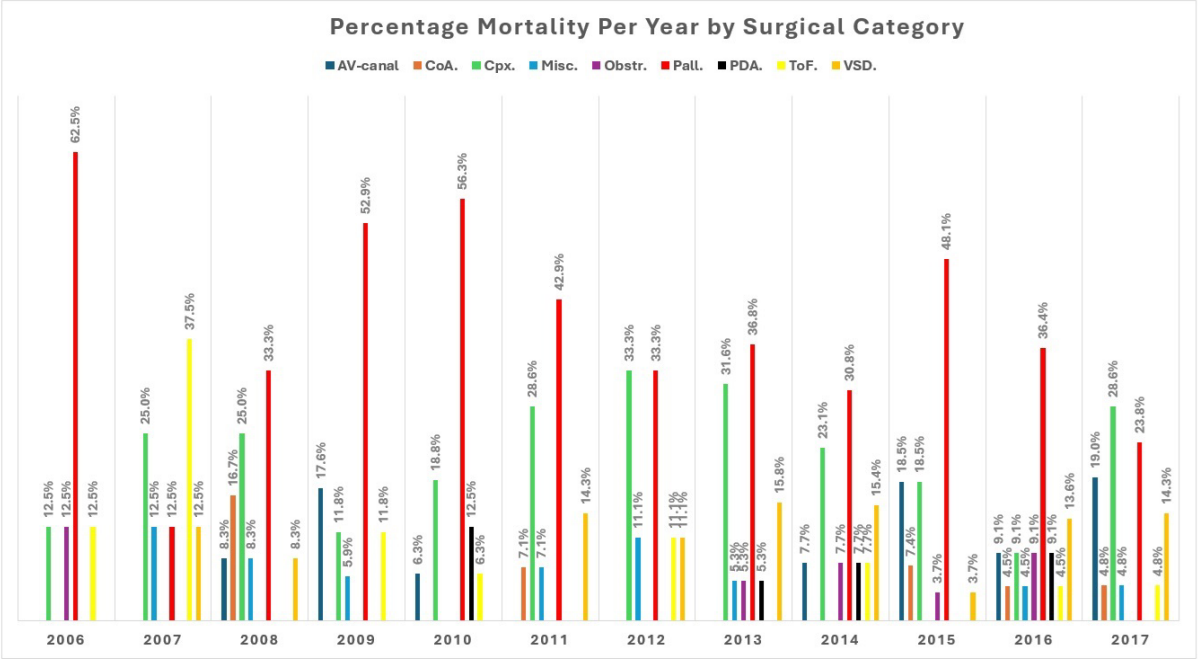
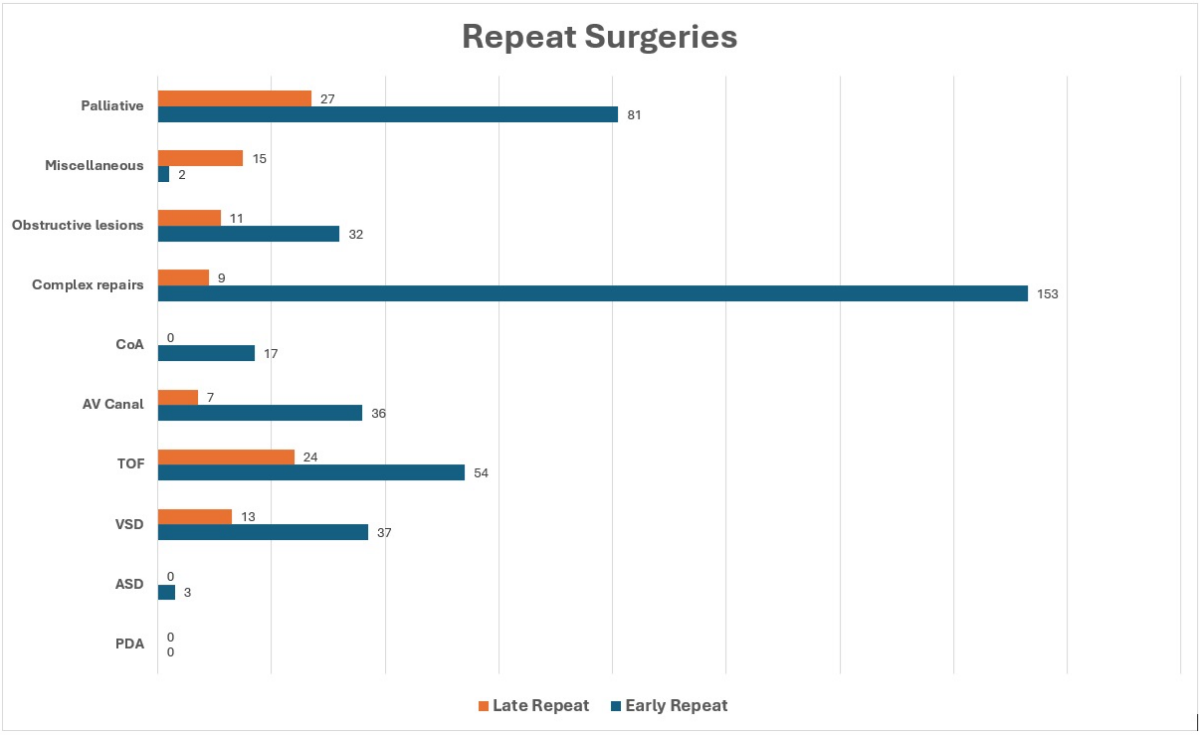
4.74
10.16
6.63
10.98
11.17
8.75
%Mortality
%Survival

Figure 2

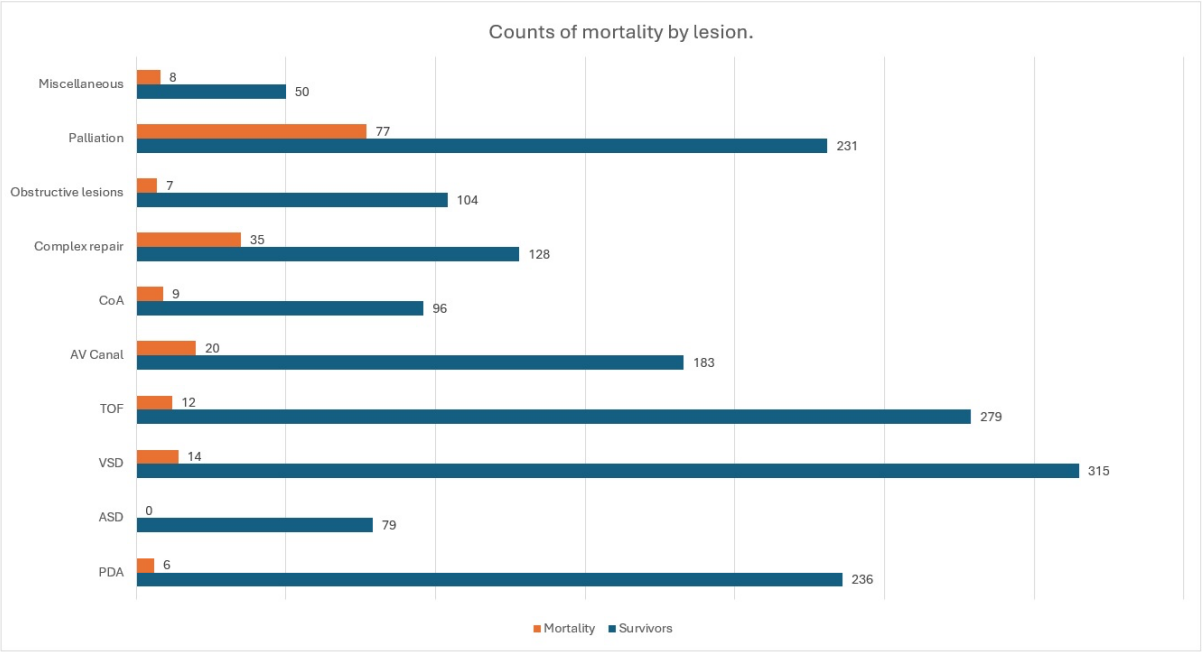


*PDA – patent ductus arteriosus, † ASD – atrial septal defect, ‡ VSD – ventricular septal defect, § CoA – coarctation of the aorta

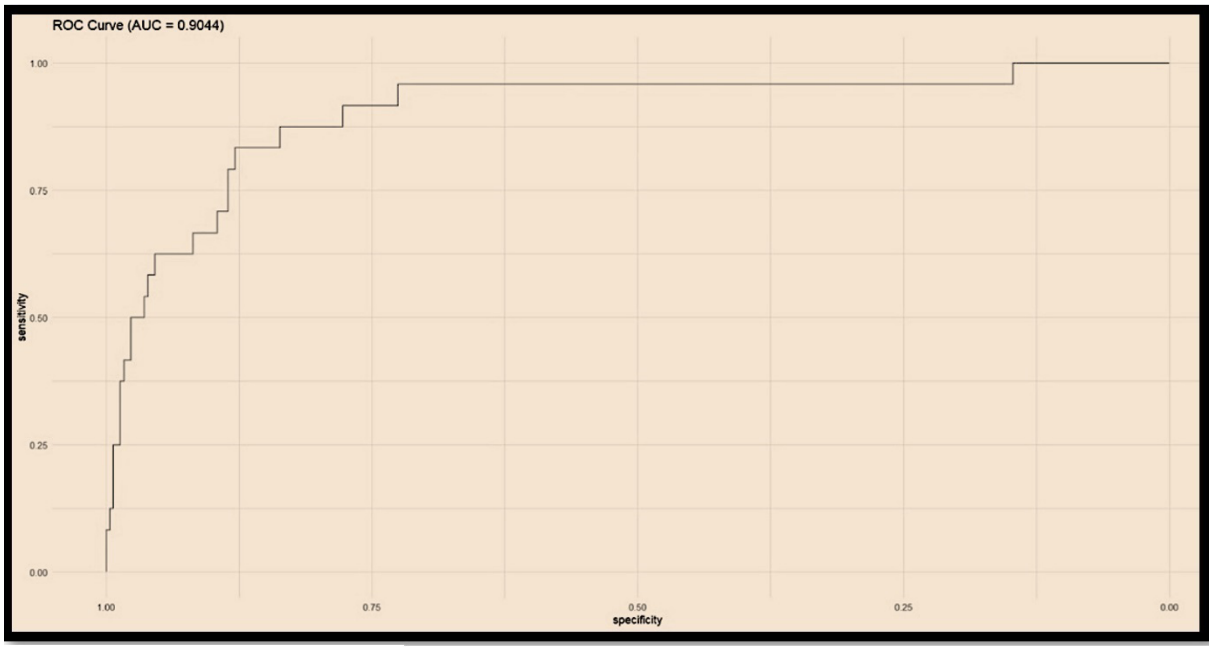
Figure 3



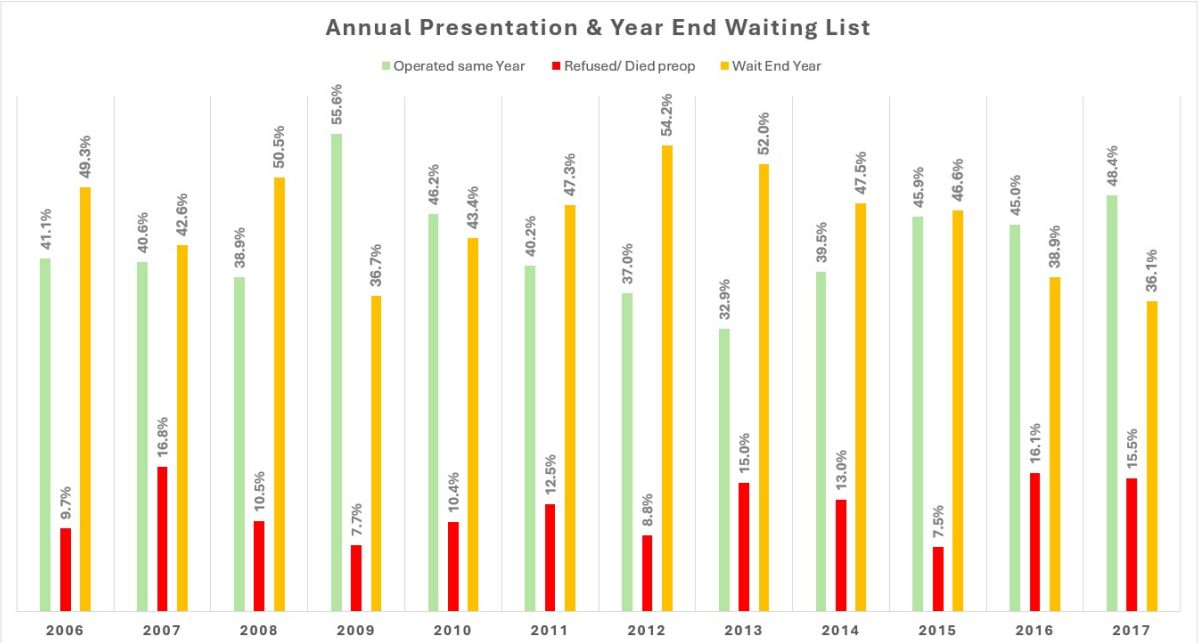
Supplementary figure 1



Supplementary figure 2



Supplementary Figure 3. The ROC Curve for the Multivariable Regression Model



Supplementary figure 4

Supplementary Table 1- Sample size computation criteria

	Samp_size	Shrinkage	Parameter	CS_Rsq	Max_Rsg	Nag_Rsq	EPP
Criteria 1	124	0.9	10	0.5	0.675	0.74	3.1
Criteria 2	208	0.937	10	0.5	0.675	0.74	5.2
Criteria 3	289	0.937	10	0.5	0.675	0.74	7.22
Final	289	0.937	10	0.5	0.675	0.74	7.22

Supplementary Table 2- Statistics for patients presentations and surgeries performed

Year	**Total Presented**	***Operated Same Yea***	***Refused/Died preop***	***Awaiting Surgery by Year End***
2006	207	85(41.1%)	20(9.7%)	102(49.3%)
2007	202	82(40.6%)	34(16.8%)	86(42.6%)
2008	190	74(38.9%)	20(10.5%)	96(50.5%)
2009	207	115(55.6%)	16(7.7%)	76(36.7%)
2010	212	98(46.2%)	22(10.4%)	92(43.4%)
2011	256	103(40.2%)	32(12.5%)	121(47.3%)
2012	273	101(37.0%)	24(8.8%)	148(54.2%)
2013	246	81(32.9%)	37(15.0%)	128(52.0%)
2014	276	109(39.5%)	36(13.0%)	131(47.5%)
2015	266	122(45.9%)	20(7.5%)	124(46.6%)
2016	298	134(45.0%)	48(16.1%)	116(38.9%)
2017	310	150(48.4%)	48(15.5%)	112(36.1%)
Average	246	105(42.6%)	30(12%)	111(45.4%)

Supplementary Document of definitions of terms used (research assumptions) for this study

PDA: = closure of patent ductus arteriosus, includes

Closure of isolated PDA, either by ligation or division
Closure of PDA with removal of device
Partial closure of PDA (done in cases with severe Pulmonary hypertension
Closure of PDA only in a case where there is a large PDA + another intracardiac lesion, as a staged procedure. The PDA is done first, and the intracardiac lesion done at later stage, either during the same admission or during a later admission

ASD: = closure of atrial septal defect with or without repair of partial anomalous pulmonary venous drainage (PAPVC). It included several associated lesions.
Partial AV canal or ASD primum is excluded.

Patch or primary closure of ASD
Patch closure of sinus venosus defect
Repair PAPVC with or without associated ASD
Closure ASD + PDA ligation
Closure ASD + mitral valve repair
Closure ASD + repair of branch PA stenosis
Closure ASD + removal of device

VSD: = Closure of ventricular septal defect ± repair of associated lesions.

Patch or primary closure VSD
Closure VSD + removal MPA band + repair MPA
Closure VSD + PDA ligation
Closure VSD + aortic valve repair / Aortic valve replacement
Closure VSD + mitral valve repair / mitral valve replacement
Closure VSD + excision supramitral membrane
Closure VSD + resection DSAS
Closure VSD + repair of pulmonary vein obstruction
Closure VSD + excision tricuspid valve

Closure VSD + atrial septectomy

PDA division or ligation, closure ASD secundum and ventricular septal defects are considered true corrective procedures. There should be no further surgery needed for these conditions, except in circumstances where the patch used dehisces or becomes infected.
All other congenital lesions have repairs, which is the closest to have a fairly normal heart or at least normal haemodynamics, but there is always the possibility that these patients will need further interventions.

AV canal: = repair of atrio-ventricular canal. It includes:

Partial AV canal or ASD primum (usually with repair of the "cleft AML")
Septation of common atrium
Partial AV canal inlet VSD (usually with repair of the "cleft AML")
Transitional AV canal
Complete AV canal
Complete AV canal + tetralogy or valvar pulmonary stenosis

Post repair of AV canal, even if initially a good repair, there is always a possibility for the child to represent with mitral or tricuspid regurgitation, and if haemodynamically significant, repeat surgery will be necessary either to re-repair the mitral valve or to replace the valve. Heart block is another long term problem post repair AV canal, for which a pace maker will be needed.

Coarctation of the Aorta:
Several types of CoA repairs are possible: patch aortoplasty, subclavian flap, resection + end to end anastomosis, resection + extended end to end anastomosis, and interposition graft. All these types or repair can be done in the following situations:

Isolated Coarctation	
	One of the above CoA repairs will be used depending on age, and anatomy
CoA + VSD	
	Repair of CoA + closure of VSD can be done as a 1 stage procedure where the 2 lesions are corrected within the same operation time

	It can also be done as a staged procedure, where the CoA is done first, and the VSD closed at a later stage, either during the same hospital admission or at a later date.
	Another possibility is the repair the CoA, and band the pulmonary artery. Closure of the VSD + debanding of the MPA will be done during a later readmission
CoA + complex Lesions	
	Often done as a staged procedure, with repair of the CoA first with a PA band. The complex lesions to be addressed at a subsequent admission
CoA as part of a Shone's complex	
	The CoA is usually done first, and the other obstructive lesions done at a later stage
	Occasionally, in an older child, the CoA and other obstructive lesions could be done in one very carefully planned procedure

Coarctations of the aorta post repair, can re-stenose or develop an aneurysm at the level of the repair. Patients with CoA have an underlying vasculopathy and need life long follow up.

Obstructive: = "Obstructive lesions + congenital valve lesions". This category includes a variety of lesions: left ventricular outflow tract obstructive lesions (LVOTO), right ventricular outflow tract obstructive lesions (RVOTO), congenital mitral valve problems: stenosis or regurgitation, tricuspid valve problems, and some other obstructive problems

LVOTO	
	Subvalvar stenosis or DSAS = discrete subaortic stenosis
	Valve aortic stenosis
	Supravalvar aortic stenosis
	Sinus of Valsalva aneurysm
RVOTO	
	Isolated pulmonary stenosis
	Double chamber RV
Mitral valve	
	Cleft mitral valve
	Supramitral membrane
	Other causes of congenital MR or MS

Tricuspid valve	
	Congenital tricuspid stenosis or regurgitation
	Ebsteins is a difficult entity as there are several degrees of Ebsteins; could also be in "Complex Lesions" and when they present in the neonatal period, a palliative procedure may be performed
Other	
	Repair cor triatriatum
	Repair pulmonary venous obstruction
	Repair systemic venous obstruction

Tetralogy: Tetralogy is a spectrum, for which there are a variety of surgical procedures, dependant on the severity of the right ventricular outflow tract obstruction. Tetralogies repaired with a transannular patch or a RV to PA conduit will come back later for repeat surgery, either a pulmonary valve replacement or a redo conduit.

Double Chamber Right Ventricle (DCRV) + VSD: closure of VSD + resection of DCRV	
Tetralogy: surgical techniques, always includes closure of VSD	
	Resection infundibular stenosis + RVOT patch
	Resection infundibular stenosis + pulmonary valvotomy
	Resection infundibular stenosis + transannular patch (tap)
	Resection infundibular stenosis + RV to PA conduit
Tetralogy with absent pulmonary valve	
Redo tetralogy, either PVR or redo RV to PA conduit	

Tetralogies with hypoplastic pulmonary arteries, and pulmonary atresia + VSD often have an initial BT shunt, and are repaired later.

Complex: this is a heterogeneous group, which includes a variety of lesions. These were grouped due to their infrequent presentation on a yearly basis.

Transposition of the great vessels	
	Repair by atrial switch or physiological correction = Mustard
	Repair by arterial switch or anatomical correction, with or without closure of VSD

Congenitally corrected TGV (ccTGV)	
DORV	
	Without PS: Intraventricular baffle
	With PS: corrected as a tetralogy
	With TGV: arterial switch
TAPVC = total anomalous pulmonary connection	
	Cardiac, supracardiac, infracardiac
Truncus	
	Truncus / or truncus with interrupted aortic arch
	Redo truncus: truncal valve replacement
	Redo truncus: redo RV to PA conduit
ALCAPA = anomalous left coronary artery from Pulmonary artery	
Interrupted aortic arch	
	Type A, B, or C
	With closure of VSD
	With PA band
RPA or LPA from ascending aorta	
Pulmonary artery sling	
Aorto-pulmonary window	
Anomalous systemic venous return	
Coronary-cameral fistula	
Ventricular inversion	

Palliation: Palliative procedures may be done for biventricular lesions, followed usually by a repair of the lesions. These are staged for univentricular hearts.

Biventricular lesions	
	PA banding in VSD or AV canal
	Shunt in tetralogy, pulmonaru atresia + VSD
	Also transannular patch without closing VSD in tetralogy
	Atrial septectomy in TGV
Univentricular lesions	

	1st stage: shunt, PA banding, Norwood, DKS ± atrial septectomy
	2nd stage: bidirectional Glenn
	3rd stage: Fontan
Neonatal Ebstein	
	Closure of tricuspid valve + shunt

Miscellaneous: A heterogenous group, usually procedures where CPB not needed

Vascular rings
Congenital heart block
Tumour resection or biopsy
Pericardial procedures

Early reoperations: Repeat open or closed heart surgery. This excludes surgical complications like bleeding, septic wounds, or planned relooks like delayed sternal closure. These are reoperations done within the same hospital admission:

Staged procedures	
	Repair CoA followed by closure VSD a few days later
	PDA ligation followed by repair of intracardiac lesion
	PA band, then closure VSD
Repair residual or recurrent lesions	
	Residual VSD post closure VSD or repair tetralogy
	Significant MR post repair AV canal or cong MR
Repair residual lesions with haemodynamic compromise – salvaged procedures	
	Pts unstable post initial op, may or not be on ECMO / LVAD Reoperation done in attempt to save patient
Revision surgery (?to be classified as residual leasions)	
	Adjustment PA band, revision Fontan
Complications	
	Blocked shunt

Late reoperations: Repeat closed or open heart surgery done months or years later.

Staged procedures: Palliation followed by repair	
VSD	Repair CoA / PA band on first admission followed by closure VSD at later stage
Shones	CoA repair initially / repair AS or MS at later stage
ToF / PA+VSD	BT shunt followed by repair later
AV canal + ToF	BT shunt initially with repair later
UVH	Repaired in stages (1st stage, Glenn, Fontan)
Repair residual lesions or recurring lesions	
DSAS	Recurring DSAS
MV repair / MVR	Post previous MV repair in AV canal or cong MR
Revision surgery	
	Redo shunt, redo PA band,
Complications of previous surgery	
	Following repair ALCAPA, arterial switch
Pacemakers need regular change of pacemaker generator (flat battery)	
Planned Redo	
Previous RV to PA conduit (truncus)	Will need replacement of the conduit when conduit degenerates
ToF, tap*	Pulm valve replacement
ToF, conduit	Redo conduit for degenerated conduit
Isolated PS	Initially pulm valvotomy or tap* / PVR at later stage
tap*	Transannular patch

Section 3: Proposal

Perioperative outcomes of paediatric congenital cardiac surgery in Johannesburg, South Africa

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3.1 Background

Congenital cardiac diseases are the most common congenital birth defects with a global incidence of between 4 - 8 cases per 1000 live births (1–4). The prevalence in South Africa is known to be no different with an incidence of between 4 - 6 per 1000 live births and approximately 11000 children born each year with congenital heart disease of which 40% require surgical intervention (5,6) An audit done by Hoosen et al (5) in 2010 showed that there are five major public centres in South Africa that offer comprehensive paediatric cardiac services. These centres include the Johannesburg complex (Chris Hani Baragwanath and Charlotte Maxeke Academic Hospitals), Steve Biko Academic Hospital, Universitas Academic Hospital, Inkosi Albert Luthuli Central Hospital and the Western Cape paediatric cardiac services (Red Cross and Tygerberg Hospitals). Approximately 1370 surgeries for congenital heart disease were performed over a one year period with only 800 being performed in the public sector.

Paediatric and neonatal cardiac surgical care is an evolving field in the developing world with a paucity of outcome data from the African continent (7). Paediatric cardiac surgical services are unable to meet the demand primarily due to a lack of skills and resources and this in turn compounds the burden of disease in South Africa. A large proportion of patients with congenital heart disease never receive treatment as a result of a number of contributing factors such as delayed referral, lack of specialised centres to perform cardiac surgery, shortage and “brain-drain” of trained specialists, cost and inadequate investment in health (1). These issues are not unique to South Africa; they exist in a number of developing countries around the world (1). In India, less than 5% of babies born with critical congenital cardiac disease undergo surgery (8). A more dire situation exists in Indonesia with less than 1% of children born with congenital cardiac disease receiving proper treatment (9).

With the developments and advances in paediatric cardiac surgical services, there have been a number of studies looking at the perioperative outcomes of paediatric congenital cardiac surgery (10–12). The majority of these studies analysed primarily mortality amongst paediatric patients undergoing congenital cardiac surgery. It was found that the more complex the surgery, the higher the mortality. It was also noted that the centres that

performed a higher volume of cases over time had a lower mortality rate (13). This was attributed to the experience of the surgeons as a result higher case exposure. It was also found that countries classified as developing countries had a higher morbidity and mortality (1,10). The reasons for this increase in morbidity and mortality were, amongst other things, attributed to the delayed referral of patients, shortage of trained specialists, cost factor and inadequate investment in health (1). Unfortunately, there is a paucity of data from the African continent. This, in part, could be attributed to the limited cardiac surgery that is being performed on the continent. Much of Africa relies on flying paid or Non-Governmental Organisation funded patients to certain centres in Africa or more commonly to developed countries in order to obtain much needed cardiac surgery (14). One of the rare and privileged centres that performed cardiac surgery on paediatric patients, until 2018, is Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

Developed countries, primarily in North America and Europe, have intuitive initiatives in place that record paediatric and congenital cardiac surgery outcome data in large databases (15). Many of these databases recorded data such as age, weight of patient, cardio-pulmonary bypass time, length of stay and in-hospital and 30-day mortality amongst other data. Some of these databases also utilised risk adjustment methods in order to easily risk stratify patient's undergoing certain surgeries. The most popular method utilised was one created by K. Jenkins et al called the Risk Adjustment for Congenital Heart Surgery (RACHS-1) (4). This method was created to improve the understanding of differences in mortality among patients undergoing congenital heart surgery. The RACHS-1 method was created by an 11 member expert panel, who strategically risk stratified 207 surgical procedures into 6 risk categories. Procedures in risk category 1 had the lowest predicted mortality and procedures in risk category 6 had the highest predicted mortality.

Another, less popular method for risk stratification is the Aristotle Basic Complexity score (ABC). This method also risk stratifies procedures from lowest to highest mortality risk in a similar fashion to the RACHS-1 method. Jacobs et al utilised both methods and concluded that complexity stratification is indeed a useful strategy for analysing the impact of case mix on paediatric cardiac surgical outcomes (17). One single centre's retrospective study in a developing country, Brazil, utilized the RACHS-1 score to risk stratify and analyse mortality

among patients that underwent surgery for congenital heart disease and found that the scoring system has a good ability to discriminate mortality (10).

With the rarity of facilities that perform paediatric cardiac surgery and paucity of data from the African continent, It is important to utilise and interpret the outcome data that is available to us at CMJAH in order to get a better understanding of how this facility, and South Africa as a whole, compare with other low to middle-income and high-income countries around the world. With this information in mind, it is quite clear that the analysis of paediatric cardiac surgical outcomes is quintessential in our setting due to the limited data from South Africa with no previous study that could be found that looked at outcomes. It will be of significant value and imperative to compare the outcomes from this study with other similar studies done around the world, and in turn utilise this data to improve paediatric cardiac surgical services in our country.

3.2 Problem statement

Paediatric cardiac surgical services are a rarity in the developing world, as is the case in South Africa even though numerous advances have been made in recent times due to the advances in technology. While progress has been made to increase the number of surgical services, there are limited studies done to show the outcomes of paediatric congenital cardiac surgery. This study will thus collect and analyse the paediatric congenital cardiac surgery data from CMJAH, in order to determine the outcomes of these surgeries.

3.3 Aim

This study aims to describe the clinical characteristics and the perioperative outcomes in paediatric patients with congenital cardiac defects requiring cardiac surgery at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

3.4 Objectives

The objectives of this study are to:

- Determine the incidence of in-hospital mortality in paediatric (age < 18 years) patients undergoing congenital cardiac surgery at CMJAH between January 2006 to December 2017.

- Determine the in-hospital mortality rates associated with particular surgical procedures.
- Describe surgical mortality in patients with congenital heart disease using the Risk Adjustment for Congenital Heart Surgery 1 (RACHS1) score in addition to the Aristotle Basic Score category (ABC) and Society of Thoracic Surgeons-European Association for Cardio - Thoracic Surgery (STS-EACTS) mortality category.

3.5 Research assumptions

The following definitions will be used in the study:

Paediatric patient: Patient < 18 years of age.

Congenital Cardiac surgery: In this study refers to all children with underlying congenital cardiac defects

RACHS 1 Score: Risk adjustment in congenital heart surgery 1, a categorical risk based classification of surgical procedures used to compare in hospital mortality in paediatric patients undergoing surgery for congenital heart disease as created by Jenkins et al (16).

ABC Score: Aristotle basic complexity score, a complexity stratification system that categorises cardiac surgical procedures according to the potential for mortality, potential for morbidity and technical difficulty.

STS-EACTS Score: Newest of the three scores devised in 2008 by the European Association for Cardiothoracic Surgery and the Society of Thoracic Surgeons. It is a mortality score that was developed primarily using objective data. This score stratifies data according to data from the STS-EACTS multicentre database.

In-hospital mortality: In this study refers to the mortality that occurs during or after the completion of cardiac surgery prior to discharge from hospital.

Perioperative outcomes: In this study refers to surgical outcomes, primarily in-hospital mortality, prolonged hospital stay, prolonged ICU stay as well as complications such as sepsis, neurological injury, renal failure and haemorrhage.

Renal Failure: In this study refers to severe renal dysfunction that requires peritoneal dialysis.

Respiratory failure: Prolonged ventilation that lasts for more than 72 hours.

Sepsis/infection: Elevated septic markers necessitating the use of antibiotics

Neurological injury: Refers to major injury such as stroke/brain damage or severe neurological fallout and seizures.

Bleeding/Haemorrhage: Refers to bleeding that warrants a relook surgery as determined by the attending surgeon.

Mechanical support: Refers to the use of extracorporeal membrane oxygenation – ECMO or ventricular assist devices.

Delayed sternal closure: Patient that underwent surgery in which the sternum was left open postoperatively.

Other complications: Refers to other miscellaneous complications such as arrhythmias and atrio-ventricular block.

3.6 Demarcation of study field

This retrospective study will include patient's clinical and surgical records from the paediatric cardiothoracic department at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) for a 12 year period from January 2006 to December 2017. CMJAH is a tertiary academic hospital that serves the public sector in the province of Gauteng. Paediatric cardiac surgical services were terminated at this hospital in December 2017. This 12 year period was used for ease of access to electronic data. An average of 150 paediatric congenital cardiac surgeries took place per year at CMJAH.

3.7 Ethical considerations

Approval and permission to conduct this study will be obtained from the Human Research Ethics Committee (HREC) and the Graduate Studies Committee of the University of the Witwatersrand (Faculty of Health Sciences).

The Chief Executive Officer of CMJAH and the departmental heads of Paediatric Cardiothoracic Surgery and Anaesthesiology will be approached to gain consent to conduct this research at this hospital (Appendix A & B). Patient's data will be treated with utmost confidentiality and anonymity will be maintained by the removal of patient identifiers and replaced by study numbers. Raw data will only be accessible by the researcher and supervisor via a personal computer which will be password protected. This raw data will be securely stored for a period of 6 years following the completion of the study.

In view of the retrospective nature of this study, informed consent from the patients is not required as there is no direct interaction with the patients. Ethical principles as governed by the South African Guidelines for Good Clinical Practice (18) and the Declaration of Helsinki (19) will be strictly followed.

3.8 Research Methodology

3.8.1 Research design

This study will be a retrospective analysis of outcome data. The study will make use of existing medical records. A descriptive retrospective case series can be used to study the incidence of a particular disease or outcome (20) as is the case in this study. The study will review records from the paediatric cardiothoracic surgery department's records in order to determine the outcome of the cases. Although a prospective study is considered superior to a retrospective one (20) in light of the termination of paediatric cardiac surgical services in this facility, it is quintessential to collect and interpret the existing medical records in a retrospective fashion.

3.8.2 Study population

Our sample population will consist of patients with congenital heart disease in the paediatric population (age < 18) that underwent cardiovascular surgery at CMJAH between January 2006 and December 2017.

3.8.3 Study sample

3.8.3.1 Sample size

In view of the retrospective nature of the study, a formal sample size is not necessary. The study will include patients that underwent cardiac surgery from 01/01/2006 – 21/12/2017. Approximately 150 cardiac surgeries took place on a yearly basis during this period.

3.8.3.2 Sampling method

Sampling is done to predict outcomes or trends in a population. This study will utilise a consecutive, convenience sampling method. Consecutive sampling aims to include all available individuals in the sample population and is the best form of convenience sampling (21).

3.8.3.3 Inclusion criteria

The inclusion criteria of this study will be:

- All paediatric (age < 18) patients that underwent congenital cardiac surgery at CMJAH from the period of 01/01/2006 to 31/12/2017.

3.8.3.4 Exclusion criteria

The exclusion criteria of this study will be:

- Patient records with incomplete data that renders it unsuitable for the study.
- Patients transferred out to other facilities. Outcomes therefore cannot be determined.
- Patients undergoing trauma surgery.
- Patients that underwent cardiac surgery other than congenital heart disease correction.

3.9 Data collection

Permission will be sought from the relevant departments involved to conduct the study. The data will be collected by the primary researcher or a trained research assistant when the researcher is unavailable.

A data collection sheet will be utilised to collate the data (Appendix C). Demographic and clinical data will be collected. Records of patients will be identified and allocated a study number. Patient identifiers will be replaced by the study number and will only be accessible by the primary researcher and supervisor. The raw data will then be captured in a Microsoft excel spreadsheet for ease of analysis.

3.10 Data analysis

Data collated on Microsoft Excel will be analysed with the assistance of a biostatistician. Data will be analysed using Stata 16 [Stata Corp LP Statistics/Data Analysis Copyright 1985 – 2013 Stata Corp 4905 Lakeway Drive Special Edition College Station, Texas 77845 USA 800– STATA]. Categorical data will be analysed using percentages and frequencies. Continuous variables will be reported with the use of mean (standard deviation), medians (interquartile range) depending on distribution. Relationships between perioperative outcomes, such as mortality, patients characteristics and risk stratification scores (RACHS 1, ABC and STS-EACTS) will be compared using paired and unpaired Student's t-tests for parametric data, or Mann-Whitney and Wilcoxon matched pairs for nonparametric data. Univariate and multivariate regression analysis of outcome measures with independent variables will be used for analyses. P-value of 0.05 will be accepted as significant.

3.11Significance of the study

It is estimated that there is an incidence of between 4-8 cases of congenital heart disease per 1000 live births (2–4). Paediatric cardiac surgery has been developing for several decades. With advances in technology and resources, massive strides have been made with regards to the surgical management of children born with congenital heart disease. These advances have in turn reduced the mortality and morbidity of children born with congenital heart disease. Unfortunately, these privileges of advanced resources and infrastructure are limited to developed countries (1).

Paediatric cardiac surgical services is hence also a limited resource in South Africa as identified by the audit of paediatric services in South Africa done by Hoosen et al in 2006 (6). This audit identified that 1370 operations for congenital heart disease were performed in 2006 of which 800 were in the public sector. Extrapolating from this, it was shockingly identified that less than 40% of the required surgeries were performed. The audit concluded that resources and infrastructure to detect and manage congenital heart disease in the public sector in South Africa were grossly inadequate.

With such limited resources, it is important to keep record of and analyse the invaluable data that is available with regards to paediatric cardiac surgery. No previous cardiac surgical outcome study could be found in South Africa. This study will thus give invaluable insight into the outcomes of paediatric patients that undergo cardiac surgery. We will be able to get a better understanding of the outcomes of South African patients and be able to compare the data with other similar studies conducted around the world. In addition, this study can serve as a stepping stone to further research in the field of paediatric cardiac surgery and anaesthesia.

3.12 Validity and reliability of the study

Validity of a study refers to the ability of a study to accurately identify the conclusions made and the degree to which these conclusions are justified (22). Reliability refers to the dependability and reproducibility of a study's outcome or results (22).

This study will ensure validity and reliability in the following ways:

- Appropriate data collection methods and study design will be utilised.
- All data collection will be done by the primary researcher.
- Appropriate inclusion and exclusion criteria will be used.
- Entries made into spreadsheets will be checked for accuracy.
- The expertise of a biostatistician will be utilised in order to analyse the data collected.

3.13 Potential limitations of the study

Due to the retrospective nature of this study, not all patients will have the required information or data needed. Access to certain pertinent clinical data may be limited in

retrospective studies. Another potential limitation that is linked with retrospective studies, is the inherent possibility of selection bias. The study will also only look at short term outcomes due to the ease of access of data and will not look at long term outcomes.
With these inherent limitations in mind, this study will aim to reduce the impact of these limitations by being aware and more cognisant of the avoidable limitations.

3.14 Project outline

3.14.1 Time frame

Year	2021/2022													
Month	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan 2022	Feb 2022	Mar 2022	April 2022	May 2022	June 2022	July 2022
Proposal														
Ethics approval														
Postgraduate approval														
Data collection														
Data analysis														
Submission														

3.14.2 Financial plan

Description	Price per item	Amount of items	Total
Printing proposal	R1 per page	400	R 400
Printing research report	R 1 per page	800	R 800
Binding final research report	R 20	2	R 40

Total	R 1240

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3.16 Appendices

3.16.1 Appendix A: Request to the CEO of the Hospital

Dr P Sarma

Department of Anaesthesiology

University of the Witwatersrand

drprathapsarma@gmail.com

30/09/2021

The Chief Executive Officer, CMJAH,

I am a registrar in the Department of Anaesthesiology. I am currently conducting research in order to complete my Masters of Medicine in Anaesthesiology. I would hereby like to request permission to conduct my study in the Department of Anaesthesiology and Paediatric Cardiac Surgery at Charlotte Maxeke Johannesburg Academic Hospital.

My study is entitled "Perioperative outcomes in paediatric congenital cardiac surgery in Johannesburg, South Africa." By retrospectively analysing data that is available in the respective departments, we will get a better understanding of outcomes of paediatric cardiac surgical services that were offered at the hospital.

The study is a retrospective outcome study and will require access to patient clinical data related to cardiac surgical procedures performed on them. Due to the retrospective nature of the study, consent will not be needed from patients. Anonymity of patient identifiers will be maintained at all times.

Post-graduate and ethics committee approval will be obtained prior to the conduct of this study. Due to the descriptive nature of the study, there will be no expense to the hospital.

Thanking you in advance for your assistance.

Regards,

Dr. Prathap Sarma

Registrar: Department of Anaesthesiology

3.16.2 Appendix B: Request to the HODs

Dr P Sarma

Department of Anaesthesiology

University of the Witwatersrand

drprathapsarma@gmail.com

30/09/2021

The Heads of Departments, Anaesthesiology & Cardiothoracic Surgery,

I am a registrar in the Department of Anaesthesiology. I am currently conducting research in order to complete my Masters of Medicine in Anaesthesiology. I would hereby like to request permission to conduct my study in the Department of Anaesthesiology and Paediatric Cardiac Surgery at Charlotte Maxeke Johannesburg Academic Hospital.

My study is entitled "Perioperative outcomes in paediatric congenital cardiac surgery in Johannesburg, South Africa." By retrospectively analysing data that is available in the respective departments, we will get a better understanding of outcomes of paediatric cardiac surgical services that were offered at the hospital.

The study is a retrospective outcome study and will require access to patient clinical data related to cardiac surgical procedures performed on them. Due to the retrospective nature of the study, consent will not be needed from patients. Anonymity of patient identifiers will be maintained at all times.

Post-graduate and ethics committee approval will be obtained prior to the conduct of this study. Due to the descriptive nature of the study, there will be no expense to the respective departments.

Thanking you in advance for your assistance.

Regards,

Dr. Prathap Sarma

Registrar: Department of Anaesthesiology

3.16.3 Appendix C: Data collection sheet

Section 1: Demographics & personal details

1. Study number
2. Age
    - In months/years
3. Gender
    - Male
    - Female
4. Ethnicity
    - Black
    - Asian
    - White
    - Mixed Ancestry
5. Weight (At the time of surgery)
    - Kilograms

Section 2: Clinical data

1. Presence of Chromosomal disorder
    - Yes
    - No
2. Preoperative length of stay (days)
3. Preoperative Cyanotic/ Acyanotic
4. Cardiac surgical procedure
    - Name of surgery conducted
    - Preoperative condition (emergent)
    - Index procedure Y/N
    - Redo procedure Y/N
    - Staged procedure Y/N
5. Surgical access route
    - Complete median sternotomy
    - Right thoracotomy

6. RACHS – 1 category (as described by Jenkins et al (23) Table 1
7. Society of Thoracic Surgeons-European Association for Cardio - Thoracic Surgery (STS-EACTS) mortality category (24) – Table 2
8. Aristotle Basic Score (ABC) Category (24) – Table 3

Section 3: Outcomes

1. Survival to hospital discharge
    - Yes
    - No
2. Length of ICU stay
    - Days
3. Length of hospital stay
    - Days
4. In hospital mortality
    - Yes
    - No
5. Cardio-pulmonary bypass used
    - Yes
    - No
6. Cardio-pulmonary bypass time
    - Minutes

Section 4: Complications

1. Renal Failure
2. Respiratory Failure
3. Poor Cardiac Output
4. Infection/Sepsis
5. Neurological Injury
6. Bleeding
7. Mechanical support
8. Delayed sternal closure

9. Other

Table 1 – Procedures by RACHS – 1 Category	
RACHS – 1 Category	Procedures
Risk Category 1	o Atrial septal defect surgery (including atrial septal defect secundum, sinus venosus atrial septal defect, patent foramen ovale closure) o Aortopexy o Patent ductus arteriosus surgery at age >30 d o Coarctation repair at age >30 d o Partially anomalous pulmonary venous connection surgery
Risk Category 2	o Aortic valvotomy or valvuloplasty at age >30 d. o Subaortic stenosis resection o Pulmonary valvotomy or valvuloplasty. o Pulmonary valve replacement. o Right ventricular infundibulectomy. o Pulmonary outflow tract augmentation. o Repair of coronary artery fistula. o Atrial septal defect and ventricular septal defect repair. o Atrial septal defect primum repair. o Ventricular septal defect repair. o Ventricular septal defect closure and pulmonary valvotomy or infundibular resection. o Ventricular septal defect closure and pulmonary artery band removal. o Repair of unspecified septal defect. o Total repair of tetralogy of Fallot. o Repair of total anomalous pulmonary veins at age >30 d Glenn shunt. o Vascular ring surgery. o Repair of aorta-pulmonary window. o Coarctation repair at age ≤30 d. o Repair of pulmonary artery stenosis. o Transection of pulmonary artery. o Common atrium closure. o Left ventricular to right atrial shunt repair.

Risk Category 3	○ Aortic valve replacement ○ Ross procedure ○ Left ventricular outflow tract patch ○ Ventriculomyotomy ○ Aortoplasty ○ Mitral valvotomy or valvuloplasty ○ Mitral valve replacement ○ Valvectomy of tricuspid valve ○ Tricuspid valvotomy or valvuloplasty ○ Tricuspid valve replacement ○ Tricuspid valve repositioning for Ebstein anomaly at age >30 d ○ Repair of anomalous coronary artery without intrapulmonary tunnel ○ Repair of anomalous coronary artery with intrapulmonary tunnel (Takeuchi) ○ Closure of semilunar valve, aortic or pulmonary ○ Right ventricular to pulmonary artery conduit ○ Left ventricular to pulmonary artery conduit ○ Repair of double-outlet right ventricle with or without repair of right ventricular obstruction ○ Fontan procedure ○ Repair of transitional or complete atrioventricular canal with or without valve replacement ○ Pulmonary artery banding ○ Repair of tetralogy of Fallot with pulmonary atresia ○ Repair of cor triatriatum ○ Systemic to pulmonary artery shunt ○ Atrial switch operation ○ Arterial switch operation ○ Reimplantation of anomalous pulmonary artery ○ Annuloplasty ○ Repair of coarctation and ventricular septal defect closure ○ Excision of intracardiac tumor
Risk Category 4	○ Aortic valvotomy or valvuloplasty at age ≤30 d ○ Konno procedure ○ Repair of complex anomaly (single ventricle) by ventricular septal defect enlargement ○ Repair of total anomalous pulmonary veins at age ≤30 d ○ Atrial septectomy

	○ Repair of transposition, ventricular septal defect, and subpulmonary stenosis (Rastelli) ○ Atrial switch operation with ventricular septal defect closure ○ Atrial switch operation with repair of subpulmonary stenosis ○ Arterial switch operation with pulmonary artery band removal ○ Arterial switch operation with ventricular septal defect closure ○ Arterial switch operation with repair of subpulmonary stenosis ○ Repair of truncus arteriosus ○ Repair of hypoplastic or interrupted arch without ventricular septal defect closure ○ Repair of hypoplastic or interrupted aortic arch with ventricular septal defect closure ○ Transverse arch graft ○ Unifocalization for tetralogy of Fallot and pulmonary atresia ○ Double switch
Risk Category 5	○ Tricuspid valve repositioning for neonatal Ebstein anomaly at age ≤30 d ○ Repair of truncus arteriosus and interrupted arch
Risk Category 6	○ Stage 1 repair of hypoplastic left heart syndrome (Norwood operation) ○ Stage 1 repair of nonhypoplastic left heart syndrome conditions ○ Damus-Kaye-Stansel procedure

Table 2 - STS-EACTS Mortality category			
	Procedure	Mortality Score	Mortality Category
1	ASD repair, patch	0.1	1
2	AVC (AVSD) repair, partial (incomplete) (PAVSD)	0.1	1
3	ASD repair, patchþ PAPCV repair	0.2	1
4	Aortic stenosis, subvalvar, repair	0.2	1
5	ICD (AICD) implantation	0.2	1
6	DCRV repair	0.2	1

7	ASD repair, primary closure	0.2	1
8	VSD repair, patch	0.2	1
9	Vascular ring repair	0.2	1
10	Coarctation repair, end to end	0.2	1
11	ICD (AICD) procedure	0.2	1
12	PFO, primary closure	0.2	1
13	AVR, bioprosthetic	0.3	1
14	VSD repair, primary closure	0.3	1
15	PVR	0.3	1
16	Conduit reoperation	0.3	1
17	Pacemaker procedure	0.3	1
18	PAPVC repair	0.3	1
19	TOF repair, ventriculotomy, nontransanular patch	0.3	1
20	TOF repair, no ventriculotomy	0.3	1
21	Glenn (unidirectional cavopulmonary anastomosis; unidirectional Glenn procedure)	0.3	1
22	AVC (AVSD) repair, intermediate (transitional)	0.3	1
23	Coarctation repair, interposition graft	0.3	1
24	Fontan, TCPC, lateral tunnel, fenestrated	0.3	1
25	Sinus of Valsalva, aneurysm repair	0.3	1
26	AVR, mechanical	0.3	1
27	PDA closure, surgical	0.4	2
28	PA, reconstruction (plasty), main (trunk)	0.4	2
29	LV to aorta tunnel repair	0.4	2
30	Valvuloplasty, mitral	0.4	2
31	Valvuloplasty, aortic	0.4	2
32	11/2 Ventricular repair	0.4	2
33	Arrhythmia surgery–ventricular, surgical ablation	0.4	2

34	Pacemaker implantation, permanent	0.4	2
35	Ross procedure	0.4	2
36	Glenn + PA reconstruction	0.4	2
37	Aortopexy	0.4	2
38	Fontan, atriopulmonary connection	0.4	2
39	Bilateral bidirectional cavopulmonary anastomosis (bilateral bidirectional Glenn procedure)	0.4	2
40	Aortic root replacement, mechanical	0.5	2
41	Conduit placement, LV to PA	0.5	2
42	Coarctation repair, end to end, extended	0.5	2
43	Anomalous origin of coronary artery repair	0.5	2
44	RVOT procedure	0.5	2
45	Aortic aneurysm repair	0.5	2
46	Congenitally corrected TGA repair, VSD closure	0.5	2
47	AP window repair	0.5	2
48	Valvuloplasty, pulmonic	0.5	2
49	TOF repair, ventriculotomy, transannular patch	0.5	2
50	Aortic root replacement, bioprosthetic	0.5	2
51	Bidirectional cavopulmonary anastomosis (bidirectional Glenn procedure)	0.5	2
52	Aortic stenosis, supravalvar, repair	0.5	2
53	Pericardiectomy	0.5	2
54	Conduit placement, other	0.5	2
55	Aneurysm, ventricular, left, repair	0.5	2
56	Fontan, TCPC, external conduit, fenestrated	0.6	2

57	Pulmonary artery origin from ascending aorta (hemitruncus) repair	0.6	2
58	ASD, common atrium (single atrium), septation	0.6	2
59	PAPVC, scimitar, repair	0.6	2
60	Fontan, TCPC, external conduit, nonfenestrated	0.6	2
61	Ligation, pulmonary artery	0.6	2
62	Coronary artery fistula ligation	0.6	2
63	Aortic root replacement, valve sparing	0.6	2
64	Mitral stenosis, supravalvar mitral ring repair	0.6	2
65	Arrhythmia surgery–atrial, surgical ablation	0.7	2
66	Systemic venous stenosis repair	0.7	2
67	PA, reconstruction (plasty), branch, peripheral (at or beyond the hilar bifurcation)	0.7	2
68	Valvuloplasty, tricuspid	0.7	2
69	TVR	0.7	2
70	Valve replacement, truncal valve	0.7	2
71	Fontan, TCPC, lateral tunnel, nonfenestrated	0.7	2
72	Atrial fenestration closure	0.7	2
73	Cor triatriatum repair	0.7	2
74	VSD, multiple, repair	0.7	2
75	Atrial baffle procedure (non-Mustard, non-Senning)	0.7	2
76	Coarctation repair, subclavian flap	0.7	2
77	Partial left ventriculectomy (LV volume reduction surgery; Batista)	0.7	2
78	TOF repair, RV–PA conduit	0.7	2
79	Transplantation, lung(s)	0.8	3
80	Occlusion MAPCA(s)	0.8	3

81	Coarctation repair VSD repair	0.8	3
82	Konno procedure	0.8	3
83	Coarctation repair, patch aortoplasty	0.8	3
84	PA, reconstruction (plasty), branch, central (within the hilar bifurcation)	0.8	3
85	Aneurysm, pulmonary artery, repair	0.8	3
86	Aneurysm, ventricular, right, repair	0.8	3
87	Ventricular septal fenestration	0.8	3
88	Shunt, ligation and takedown	0.8	3
89	Hemi-Fontan procedure	0.8	3
90	AVC (AVSD) repair, complete	0.8	3
91	Anomalous systemic venous connection repair	0.8	3
92	ASO	0.8	3
93	Valvuloplasty, truncal valve	0.8	3
94	Fontan, atrioventricular connection	0.9	3
95	Pulmonary embolectomy, acute pulmonary embolus	0.9	3
96	ASD partial closure	0.9	3
97	Rastelli operation	0.9	3
98	Conduit placement, ventricle to aorta	0.9	3
99	AVR, homograft	1.0	3
100	REV	1.1	3
101	Pulmonary artery sling repair	1.1	3
102	Mustard procedure	1.1	3
103	Pulmonary atresia–VSD (including TOF, PA) repair	1.1	3
104	Conduit placement, RV to PA	1.2	3
105	Pulmonary embolectomy	1.2	3
106	MVR	1.3	4
107	Pericardial drainage procedure	1.3	4
108	Aortic arch repair	1.4	4

109	Fontan revision or conversion (redo Fontan procedure)	1.4	4
110	DOLV repair	1.4	4
111	DORV, intraventricular tunnel repair	1.4	4
112	Arterial switch procedure+ aortic arch repair	1.4	4
113	PA debanding	1.4	4
114	ASO and VSD repair	1.4	4
115	Cardiac tumor resection	1.4	4
116	Transplantation, heart	1.4	4
117	Coronary artery bypass	1.5	4
118	TOF–absent pulmonary valve repair	1.5	4
119	Valve excision, tricuspid (without replacement)	1.5	4
120	Shunt, systemic to pulmonary, MBTS	1.5	4
121	TOF–AVC (AVSD) repair	1.6	4
122	Ross–Konno procedure	1.6	4
123	Senning procedure	1.6	4
124	Ebstein's repair	1.6	4
125	Aortic arch repair+VSD repair	1.7	4
126	PA banding	1.7	4
127	Aortic root replacement, homograft	1.7	4
128	Unifocalization MAPCA(s)	1.7	4
129	Aortic dissection repair	1.7	4
130	Congenitally corrected TGA repair, VSD closure and LV to PA conduit	1.7	4
131	Pulmonary atresia–VSD–MAPCA (pseudotruncus) repair	1.7	4
132	VSD creation/enlargement	1.8	4
133	HLHS biventricular repair	1.9	4
134	TAPVC repair	1.9	4
135	Pulmonary venous stenosis repair	2.0	4
136	Shunt, systemic to pulmonary, central (from	2.1	4

	aorta or to main pulmonary artery)		
137	Interrupted aortic arch repair	2.1	4
138	Arterial switch procedure and VSD repairþaortic arch repair	2.4	4
139	Truncus arteriosus repair	2.4	4
140	ASD creation/enlargement	2.5	4
141	Atrial septal fenestration	2.6	4
142	Valve closure, tricuspid (exclusion, univentricular approach)	2.6	4
143	Damus–Kaye–Stansel procedure (creation of AP anastomosis without arch reconstruction)	2.9	5
144	Transplantation, heart and lung	3.2	5
145	Congenitally corrected TGA repair, atrial switch and Rastelli operation	3.2	5
146	Congenitally corrected TGA repair, atrial switch and ASO (double switch)	3.4	5
147	Norwood procedure	4.0	5
148	Truncus+IAA repair	5.0	5

Table 3 - ABC Score

	Procedure	Basic Score	Complexity level
1	PFO, Primary closure	3.0	1
2	ASD repair, Primary closure	3.0	1
3	ASD repair, Patch	3.0	1
4	ASD, Common atrium (Single atrium), Septation	3.8	1
5	ASD creation/enlargement	4.0	1
6	ASD partial closure	3.0	1

7	Atrial septal fenestration	5.0	1
8	VSD repair, Primary closure	6.0	2
9	VSD repair, Patch	6.0	2
10	VSD, Multiple, Repair	9.0	3
11	VSD creation/enlargement	9.0	3
12	Ventricular septal fenestration	7.5	2
13	AVC (AVSD) repair, Complete (CAVSD)	9.0	3
14	AVC (AVSD) repair, Intermediate (transitional)	5.0	1
15	AVC (AVSD) repair, Partial (incomplete) (PAVSD)	4.0	1
16	AP window repair	6.0	2
17	Pulmonary artery origin from ascending aorta (hemitruncus) repair	9.0	3
18	Truncus arteriosus repair	11.0	4
19	Valvuloplasty, Truncal valve	7.0	2
20	Valve replacement, Truncal valve	6.0	2
21	PAPVC repair	5.0	1
22	PAPVC, Scimitar, Repair	8.0	3
23	TAPVC repair	9.0	3
24	Cor triatriatum repair	6.8	2
25	Pulmonary venous stenosis repair	12.0	4
26	Atrial baffle procedure (non-Mustard, non-Senning)	7.8	2
27	Anomalous systemic venous connection repair	7.0	2
28	Systemic venous stenosis repair	8.0	3
29	TOF repair, No ventriculotomy	8.0	3
30	TOF repair, Ventriculotomy, Non-transanular patch	7.5	2
31	TOF repair, Ventriculotomy, Transanular patch	8.0	3
32	TOF repair, RV-PA conduit	8.0	3
33	TOF—AVC (AVSD) repair	11.0	4
34	TOF—Absent pulmonary valve repair	9.3	3
35	Pulmonary atresia—VSD (including TOF, PA) repair	9.0	3
36	Pulmonary atresia—VSD—MAPCA (pseudotruncus) repair	11.0	4
37	Unifocalization MAPCA (s)	11.0	4
38	Occlusion MAPCA (s)	7.0	2
39	Valvuloplasty, Tricuspid	7.0	2
40	Valve replacement, Tricuspid (TVR)	7.5	2
41	Valve closure, Tricuspid (exclusion, univentricular approach)	9.0	3
42	Valve excision, Tricuspid (without replacement)	7.0	2
43	RVOT procedure	6.5	2
44	1 1/2 ventricular repair	9.0	3

45	PA, reconstruction (plasty), Main (trunk)	6.0	2
46	PA, reconstruction (plasty), Branch, Central (within the hilar bifurcation)	7.8	2
47	PA, reconstruction (plasty), Branch, Peripheral (at or beyond the hilar bifurcation)	7.8	2
48	DCRV repair	7.0	2
49	Conduit reoperation	8.0	2
50	Valvuloplasty, Pulmonic	5.6	1
51	Valve replacement, Pulmonic (PVR)	6.5	2
52	Conduit placement, RV to PA	7.5	2
53	Conduit placement, LV to PA	8.0	3
54	Valvuloplasty, Aortic	8.0	3
55	Valve replacement, Aortic (AVR), Mechanical	7.0	2
56	Valve replacement, Aortic (AVR), Bioprosthetic	7.0	2
57	Valve replacement, Aortic (AVR), Homograft	8.5	3
58	Aortic root replacement	8.0	3
59	Aortic root replacement, Mechanical	8.8	3
60	Aortic root replacement, Homograft	9.5	3
61	Ross procedure	10.3	4
62	Konno procedure	11.0	4
63	Ross – Konno procedure	12.5	4
64	Aortic stenosis, Subvalvar, Repair	6.3	2
65	Aortic stenosis, Supravalvar, Repair	7.5	2
66	Sinus of Valsalva, Aneurysm repair	7.5	2
67	LV to aorta tunnel repair	8.3	3
68	Valvuloplasty, Mitral	8.0	3
69	Mitral stenosis, Supravalvar mitral ring repair	8.0	3
70	Valve replacement, Mitral (MVR)	7.5	2
71	Norwood procedure	14.5	4
72	HLHS biventricular repair	15.0	4
73	Transplant, Heart	9.3	3
74	Transplant, Heart and lung(s)	13.3	4
75	Partial left ventriculectomy (LV volume reduction surgery) (Batista)	12.0	4
76	Pericardial drainage procedure	3.0	1
77	Pericardiectomy	6.0	2
78	Fontan, Atrio-pulmonary connection	9.0	3
79	Fontan, Atrio-ventricular connection	9.0	3
80	Fontan, TCPC, Lateral tunnel, Fenestrated	9.0	3
81	Fontan, TCPC, Lateral tunnel, Non-fenestrated	9.0	3
82	Fontan, TCPC, External conduit, Fenestrated	9.0	3

83	Fontan, TCPC, External conduit, Non-fenestrated	9.0	3
84	Congenitally corrected TGA repair, Atrial Switch and ASO (Double switch)	13.8	4
85	Congenitally corrected TGA repair, Atrial switch and Rastelli	11.0	4
86	Congenitally corrected TGA repair, VSD closure	9.0	3
87	Congenitally corrected TGA repair, VSD closure and LV to PA conduit	11.0	4
88	Arterial switch operation (ASO)	10.0	4
89	Arterial switch operation (ASO) and VSD repair	11.0	4
90	Senning	8.5	3
91	Mustard	9.0	3
92	Rastelli	10.0	4
93	REV	11.0	4
94	DORV, Intraventricular tunnel repair	10.3	4
95	DOLV repair	11.0	4
96	Anomalous origin of coronary artery from pulmonary artery repair	10.0	4
97	Coronary artery fistula ligation	4.0	1
98	Coronary artery bypass	7.5	2
99	Coarctation repair, End to end	6.0	2
100	Coarctation repair, End to end, Extended	8.0	3
101	Coarctation repair, Subclavian flap	6.0	2
102	Coarctation repair, Patch aortoplasty	6.0	2
103	Coarctation repair, Interposition graft	7.8	2
104	Aortic arch repair	7.0	2
105	Interrupted aortic arch repair	10.8	4
106	PDA closure, Surgical	3.0	1
107	Vascular ring repair	6.0	2
108	Pulmonary artery sling repair	9.0	3
109	Aortic aneurysm repair	8.8	3
110	Aortic dissection repair	11.0	4
111	Lung biopsy	5.0	1
112	Transplant, Lung(s)	12.0	4
113	Pectus repair	5.3	1
114	Pacemaker implantation, Permanent	3.0	1
115	Pacemaker procedure	3.0	1
116	ICD (AICD) implantation	4.0	1
117	ICD (AICD) (automatic implantable cardioverter defibrillator) procedure	4.0	1
118	Arrhythmia surgery—atrial, Surgical ablation	8.0	3

119	Shunt, Systemic to pulmonary, Modified Blalock-Taussig shunt (MBTS)	6.3	2
120	Shunt, Systemic to pulmonary, Central (From aorta or to main pulmonary artery)	6.8	2
121	Shunt, Ligation and takedown	3.5	1
122	PA banding (PAB)	6.0	2
123	PA debanding	6.0	2
124	Damus – Kaye – Stansel procedure (DKS) (creation of AP anastomosis without arch reconstruction)	9.5	3
125	Bidirectional cavopulmonary anastomosis (BDCPA) (bidirectional Glenn)	6.8	2
126	Glenn (unidirectional cavopulmonary anastomosis) (unidirectional Glenn)	7.0	2
127	Bilateral bidirectional cavopulmonary anastomosis (BBDCPA) (bilateral bidirectional Glenn)	7.5	2
128	Hemifontan	8.0	3
129	Aneurysm, Ventricular, Right, Repair	8.0	3
130	Aneurysm, Ventricular, Left, Repair	9.0	3
131	Aneurysm, Pulmonary artery, Repair	8.0	3
132	Cardiac tumor resection	8.0	3
133	Ligation, Pulmonary artery	5.0	1
134	Pulmonary embolectomy	8.0	3
135	Pleural drainage procedure	1.5	1
136	Ligation, Thoracic duct	4.0	1
137	Decortication	5.0	1
138	Intra-aortic balloon pump (IABP) insertion	2.0	1
139	ECMO procedure	6.0	2
140	Right/left heart assist device procedure	7.0	2
141	Bronchoscopy	1.5	1
142	Diaphragm plication	4.0	1
143	Delayed sternal closure	1.5	1
144	Mediastinal exploration	1.5	1
145	Sternotomy wound drainage	1.5	1

Section 4 Annexures

4.1 Supervisor approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES | WITS SCHOOL OF CLINICAL MEDICINE | DEPARTMENT OF ANAESTHESIOLOGY
Tel.(011)488 4344

21 October 2021

Postgrad Office

School of Clinical Medicine

Faculty of Health Sciences

University of the Witwatersrand

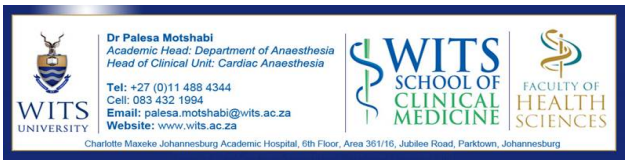
To Whom It May Concern

Proposal Approval: Dr Prathap Sarma

This is to confirm that I have read and approved **Dr Sarma's** corrections for final submission as suggested by the postgraduate committee members for his proposal towards a Mmed project titled "***Perioperative outcomes of paediatric congenital cardiac surgery in Johannesburg, South Africa***".

Thank you.

Dr P Motshabi



4.2 Anaesthesia HOD approval

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF ANAESTHESIA
Area 361
Charlotte Maxeke Johannesburg Academic Hospital

Tel: 011 488 4344
Fax: 086 765 3477

29 March 2022

Dr Prathap Sarma
Specialist / Consultant
Department of Anaesthesia
CMJAH

Dear Dr Sarma

PROPOSED MMED RESEARCH PROJECT

Your proposed research project titled "Perioperative outcomes in paediatric congenital cardiac surgery in Johannesburg, South Africa" has the potential to help us understand all related relevant factors and improve outcomes in future. The Department of Anaesthesia fully supports this study.

However, preconditions are that the study has no cost implication to the hospital, does not interfere with service delivery, and must be approved by the relevant ethics/research authorities, namely university ethics committee and hospital research committee before data collection starts.

I fully support you in this research endeavor. Looking forward to your findings.

Yours sincerely,

_____
Prof EE Oosthuizen
Clinical head: Department of Anaesthesia
CMJAH

4.3 Cardiothoracic HOD approval

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

University
of the Witwatersrand
Johannesburg

Department of Surgery:

Charlotte Maxeke Johannesburg Academic Hospital

Post net Suite #235, Private Bag x2600, Houghton 2041 • Telephone +27 (0)11 717-2536• Fax +27 (0)11 488-4322 • Email: Mandisa.Khumalo@wits.ac.za

10th January 2022

Ms. G Bogoshi
Office of the CEO
Charlotte Maxeke Johannesburg Academic Hospital

Dear CEO

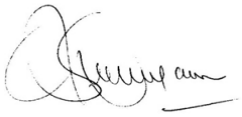
Re: Research Project:

Good day. This is to inform you that Dr P. Sarma is planning to conduct a study titled:

Perioperative outcomes of paediatric congenital cardiac surgery in Johannesburg, South Africa.

We are aware of the study and fully support it. There will be no cost implication to the Hospital. Has already applied for ethical approval from the Human Ethics Committee of University of the Witwatersrand.

Yours sincerely
SM Mogaladi (HOD)



Department of cardiothoracic surgery
University of the Witwatersrand
Faculty of Health Sciences
School of Clinical Medicine
01171712536
Shungu.mogaladi@gauteng.gov.za
Shungu.mogaladi@wits.ac.za
Shungu.mogaladi@gmail.com

4.4 CMJAH CEO Approval

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL (CMJAH)
OFFICE OF THE SENIOR CLINICAL MANAGER

Enquiries: *Ms N. Mzila*
Email: Nolwazi.Mzila@gauteng.gov.za
Tel: *011 488 3365*
Ref: *1/7/2*
Date: 7 July 2022

GP_202111_024

Dear Dr Prathap Sarma

RE: FINAL APPROVAL OF STUDY

TITLE: PERIOPERATIVE OUTCOMES OF PAEDIATRIC CONGENITAL CARDIAC SURGERY IN JOHANNESBURG, SOUTH AFRICA

Permission is granted for you to conduct the above-mentioned study as described in your request provided:

1. Charlotte Maxeke Johannesburg Academic Hospital will not in any way incur or inherit costs as a result of the said study.
2. Your study shall not disrupt services at the study sites.
3. Strict confidentiality shall always be observed.
4. Informed consent shall be solicited from patients participating in your study.

Please liaise with the HOD and Unit Manager or Sister in charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

Supported/~~Not Supported~~

_____
Dr J. Punwasi
Senior Clinical Manager

Approved/~~Not Approved~~

_____
Ms. G Bogoshi
Chief Executive Officer

4.5 Ethical approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Prathap Sarma

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M211151

NAME: (Principal Investigator)	Dr Prathap Sarma
DEPARTMENT:	Anaesthesiology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Perioperative outcomes of paediatric congenital cardiac surgery in Johannesburg, South Africa
DATE CONSIDERED:	26/11/2021
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the University Registrar's office <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Dr Palesa Motshabi-Chakane
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	11/04/2022

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. I **agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore be due in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

4.6 Graduate studies approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

22 November 2021
Person No: 437897
PAG

Dr P Sarma
Unit 10 Park Street Estate
47 Park Street
Oaklands
2192
South Africa

Dear Dr Prathap Sarma

Master of Medicine in Anaesthesia: Approval of Title

We have pleasure in advising that your proposal entitled *Perioperative outcomes of paediatric congenital cardiac surgery in Johannesburg, SouthAfrica* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

4.7 Turnitin report

Manuscript copy-1.docx

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