Title Page

Title

Transanal total mesorectal excision: Is there a problem with using case series to assess new operative techniques?

Short running head

Issues with case series assessing TaTME

Authors

Dilshan K. Udayasiri

Degrees: M.B.B.S., F.R.A.C.S.

Academic title: Dr

Main appointment:

Colorectal research fellow

Institution/department:

Colorectal Surgical Unit, The Royal Melbourne Hospital, Victoria, Australia

Department of General Surgical Specialties, The Royal Melbourne Hospital, Victoria, Australia

Department of Surgery, The University of Melbourne, Victoria, Australia

Anita Skandarajah

Degrees: M.B.B.S., M.D., F.R.A.C.S., F.A.C.S

Academic title: Dr

Main Appointment:

Breast and Endocrine Surgeon

Co Supervisor for research

Institution/department:

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ans.16507

This article is protected by copyright. All rights reserved.
Department of General Surgical Specialties, The Royal Melbourne Hospital, Victoria, Australia

Department of Surgery, The University of Melbourne, Victoria, Australia

Ian P. Hayes

Degrees: M.B.B.S., M.S., M.Epi., F.R.A.C.S., F.R.C.S. (Gen-Surg)

Academic title: Clinical Associate Professor

Main Appointment:
Chief Supervisor of Research
Head of Colorectal Surgical Unit
Colorectal Surgeon

Institution/department:
Colorectal Surgical Unit, The Royal Melbourne Hospital, Victoria, Australia
Department of General Surgical Specialties, The Royal Melbourne Hospital, Victoria, Australia
Department of Surgery, The University of Melbourne, Victoria, Australia

Author responsible for correspondence about the manuscript

Dr Dilshan Udayasiri
9 Cook Street, Ivanhoe, Victoria, Australia, postcode 3079
Telephone: +61431059868
Email: dilshan.udayasiri@gmail.com
Podium or Poster Presentations

Nil

Word count of text: 991
Number of tables and figures: 0

Disclaimers

There are no conflicts of interest in this article.
The taTME procedure, a modified technique for achieving total mesorectal excision during rectal cancer surgery, has been used for several years\(^1\). Surgeons commencing this technique have been well supported with courses and proctorship\(^2\) and encouraged to contribute outcome data to central data repositories to monitor overall results\(^3,4\). The process and governance of the introduction of this technique are well organised and are based on lessons learned from the uptake of other novel techniques such as robotic surgery. Several case series have been published showing similar results to standard surgery\(^2,4-17\). Recently, however, concern was raised following a Norwegian study which compared this technique to standard surgery as it found evidence of increased and atypical local recurrences in taTME with multifocal disease in the pelvic cavity and sidewall\(^18-20\). Moreover, taTME was associated with unusual complications, particularly urethral injuries\(^21,22\). As a result of this, The Association of Coloproctology of Great Britain and Ireland (ASCPGBI) have suggested more detailed reporting and scrutiny of future cases\(^23\).

These suggestions seem reasonable but will data from further case series provide an adequate evidence base for the introduction of this new technique?

Most surgeons are innovative practitioners and develop efficiencies and personalised variations of operative technique that suit how they practice their craft and are tailored to solving the problems they may have encountered over time. It is not feasible or necessary to submit every minor change in technique to a major clinical trial. However, rigorous analysis is required for new techniques that might be less effective or cause greater harm to patients than the current standard. The Norwegian study alerts us that there may be problems with taTME.

Evidence from case series, even when well performed, is insufficient to address the concerns raised about taTME. No study type is perfect but we must strive to minimise the sources of error which are: chance, bias and confounding.

Error source 1: chance. The main deficiency of a case series is the lack of comparison with a control group. A skilled surgeon may be able to achieve reasonable results from a new technique but may be able to achieve even better results using the standard technique. Therefore, an appropriate study should be a comparative analysis of techniques rather than a demonstration of what an individual surgeon can achieve with a specific technique. A key issue is that a comparative study allows analysis of the contribution of chance to the result, represented by the p-value. A p-value of 0.05 indicates there is a 5% probability that result could be due to random chance. Without a comparative study the p-value cannot be quantified.

Error source 2: confounding. The most obvious difference affecting outcome between two groups is the treatment received. However, there may be other differences in baseline variables between the two groups that could also affect the outcome (a.k.a. covariables). Confounding could be produced by imbalances in co-variables such as age, obesity and stage of tumour. Statistical techniques such as multivariable regression analysis or propensity score analysis can be performed to adjust for the potentially confounding effects of measurable covariables.
Error source 3: bias. Bias refers to systematic differences between treatment groups in patient selection or measurement of outcomes which could lead to erroneous results. Where there are strong motivators which encourage early adoption of new procedures (such as prestige, market share or remuneration), there is potential that the cases selected for a new procedure and presented in a case series may differ from standard patients. For example, patients may self-select (volunteer bias), referrers may seek out a surgeon at the forefront of technology for selected patients (referral bias) and surgeons may choose cases for the new procedure which are more likely to have good outcomes (selection bias). In analysing studies, bias can be suspected but is not always measurable. Unmeasurable bias cannot be adjusted for mathematically. To minimise bias, only randomisation can balance both measurable and unmeasurable covariables between groups and create groups which are exchangeable between treatments. As opposed to a case series where selection bias can play a major role, randomisation minimises the surgeon as a factor in determining treatment allocation. It is important to note that the control/comparator in a randomized controlled trial should be carefully chosen. This benchmark should represent the procedure that yields the best results for the most important outcomes (i.e. the current standard of care). One should not compare one experimental procedure to another experimental procedure or one that has been shown to be inferior to a gold-standard, for example the choice of laparoscopic TME as the control group in the current COLOR III taTME trial is questionable.

However, case series have their place. The publication of a case series by an eminent surgeon using an established technique makes for interesting reading within that craft-group and can act as a benchmark for what can be achieved. A case series can also be of significance where there is no appropriate comparator, such as RJ Heald’s initial series describing a meticulous technique of rectal dissection. A case series (before comparative studies are done) can also be relevant as a phase one study assessing the practicalities and safety profile of a new technique. However, there are now approximately 4500 taTME cases published; we are beyond initial exploratory studies.

We have used the example of taTME to illustrate the limitations and danger of using case series as the evidence base to support the use of a new surgical technique. taTME is a new operation for a serious condition with some evidence of potential to worsen outcomes and cause extra morbidity. Further case series will not provide methodologically sound answers about the utility of this procedure. Although the Norwegian study provided a higher level of evidence than case series, its findings have failed to limit the uptake of this procedure. Given the conflicting results so far, high quality randomised evidence is required to assess this technique and avoid the potentially erroneous conclusions that further case series may lead us to.


Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:
Udayasiri, DK; Skandarajah, A; Hayes, IP

Title:
Transanal total mesorectal excision: is there a problem with using case series to assess new operative techniques?

Date:
2021-05-01

Citation:

Persistent Link:
http://hdl.handle.net/11343/298517