PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Short-term morbidity and mortality following radical cystectomy: a systematic review
AUTHORS	Maibom, Sophia; Joensen, Ulla; Poulsen, Alicia; Kehlet, Henrik; Brasso, Klaus; Røder, Martin Andreas

VERSION 1 – REVIEW

REVIEWER	Peter Herbison University of Otago New Zealand
REVIEW RETURNED	19-Aug-2020

GENERAL COMMENTS	I have several concerns about this paper. The first is the inclusion and exclusion characteristics for the papers. These are far more extensive than would be normal for a systematic review. Several of these such as excluding abstracts and conference papers, and the size of the study have been shown, in systematic reviews of randomised controlled trials, to be unnecessary, and to possibly result in biased results. The authors should at the least justify their exclusions, or rethink them. The authors state what they will do if they find duplicate publications from the same study. But it would seem that most of these criteria apply to different studies rather than the same study. For example prioritising prospective over retrospective studies cannot apply to the same study. There are some new results for this study that are first reported in the discussion. In the conclusions in the manuscript (not the abstract) there is the claim "However, with thorough patient selection, experienced surgeons, treatment at a high-volume hospital and the implementation of an ERAS protocol morbidity and mortality can likely be reduced." This is not based on data from this study.

REVIEWER	Takashige Abe Hokkaido University, Sapporo, Japan
REVIEW RETURNED	17-Jan-2021

GENERAL COMMENTS	The authors performed systematic review regarding postoperative complications after radical cystectomy, and summarized the overview in narrative manner. 1. Table 1. The authors should provide the patients numbers

	regarding the surgical approach (open, laparoscopy, or robotic.) 2. Table 1. The authors should explain the details of previous radiation. Does it mean radiotherapy to bladder or any site? 3. Readmission rate is another surrogate marker in terms of postoperative complications after radical cystectomy. The authors should add the data of readmission rates within 90days after surgery. 4. The details of cause of death should be described, if possible.

VERSION 1 – AUTHOR RESPONSE

Respons to reviewer 1

Thank you for your review of our paper. A detailed response to your comments is addressed below in italic.

Prof. Peter Herbison, University of Otago
Comments to the Author:
I have several concerns about this paper.

The first is the inclusion and exclusion characteristics for the papers. These are far more extensive than would be normal for a systematic review. Several of these such as excluding abstracts and conference papers, and the size of the study have been shown, in systematic reviews of randomised controlled trials, to be unnecessary, and to possibly result in biased results. The authors should at the least justify their exclusions, or rethink them.

Thank you for the valuable comment. It is likely correct that some information can be derived from small studies, including conference abstracts. There are many small cohort studies of cystectomy in less than 100 patients, most of them are often very specific cohorts of e.g. cystectomy in octogenarians or cystectomy in a specific subset of patients with specific urinary diversions such as a new technique of a neobladder or so forth. We intended to systematically review *morbidity in a broad group of cystectomy patients, not a small subset of patients. We wanted to gather information about morbidity in larger series of patients where we could expect a certain level of experience and learning within the cohort and thus hopefully level the expected bias that affect the risk of morbidity. Was 100 patients the correct level to choose? The level was empirically chosen to balance both the number of papers needed to be screened and the learning curve that may affect the frequency of complications. The learning curve for cystectomy has long been debated, and also depends on what you wish to achieve; operation time, the number of lymph nodes, complications etc., but it may be around 25-50 cases, thus we believe 100 was relevant to address complications among experienced surgeons. Conference abstracts were excluded as they typically are copies of later published articles. Unfortunately, this is the decision that was chosen and is impossible to correct at the current stage of the publication process. Also, we must state that the problem addressed by Prof. Herbison was not addressed by PROPERO when the search string was published there.*

The authors state what they will do if they find duplicate publications from the same study. But it would seem that most of these criteria apply to different studies rather than the same study. For example, prioritising prospective over retrospective studies cannot apply to the same study.

Some retrospective cohort studies from centres included patients that were also included in a prospective study from the same centre. These studies had different objectives but sometimes reported overlapping data. Also, data from the same database (e.g. NSQIP, NIS) could be from the

same period.

There are some new results for this study that are first reported in the discussion.
We have added references from other studies to put the findings of the review into perspective. To clarify this, we have changed the wording of the text to highlight which findings are from our review and which are not.

In the conclusions in the manuscript (not the abstract) there is the claim "However, with thorough patient selection, experienced surgeons, treatment at a high-volume hospital and the implementation of an ERAS protocol morbidity and mortality can likely be reduced." This is not based on data from this study.

We have elaborated in the discussion on studies included in the review that has addressed these issues to make it more clear.

Response to reviewer: 2
Thank you for your review of our paper. We have answered each of your points below, marked in italic.

Dr. Takashige Abe, Hokkaido University Graduate School of Medicine
Comments to the Author:
The authors performed systematic review regarding postoperative complications after radical cystectomy, and summarized the overview in narrative manner.

1. Table 1. The authors should provide the patients numbers regarding the surgical approach (open, laparoscopy, or robotic.)

We have added the weighted average (and ranges) for the surgical approaches in Table 1 as requested.

2. Table 1. The authors should explain the details of previous radiation. Does it mean radiotherapy to bladder or any site?

We have specified that it is previous radiation to the pelvis not including patients receiving external beam radiation due to bladder cancer.

3. Readmission rate is another surrogate marker in terms of postoperative complications after radical cystectomy. The authors should add the data of readmission rates within 90days after surgery.

We did not include "readmissions" as an outcome as our search was already extensive. As "readmissions" was not specified in the search string or as a criterium for the selection of included studies, including a readmission rate based on included studies in our review would potentially give an inaccurate estimate.

4. The details of cause of death should be described, if possible.

We have added information on the cause of death from the papers providing this information as requested.

VERSION 2 – REVIEW

REVIEWER	Peter Herbison University of Otago New Zealand
REVIEW RETURNED	18-Mar-2021

GENERAL COMMENTS	While I still think that it is likely that too many studies have been excluded, it was at least clear what was done. One of the reasons for excluding small studies, that they were done in very specific populations, would have been better done through the description of the populations in the inclusion/exclusion criteria rather than size.