SCANDINAVIAN JOURNAL OF UROLOGY
2022, VOL. 56, NO. 1, 6–11
https://doi.org/10.1080/21681805.2021.1987978

ARTICLE

Prospective versus retrospective recordings of comorbidities and complications in bladder cancer patients undergoing radical cystectomy – a randomized controlled trial

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ABSTRACT

Background: Patients undergoing radical cystectomy are predominantly elderly with many comorbidities and high risk of complications. Studies on comorbidity and complications following cancer surgery are often based on data collected retrospectively from records. However, prospective registration is often considered a more valid source of information. Therefore, it is relevant to investigate if the amount and severity of complications and comorbidities is valid when using retrospective registration compared to a more meticulous prospective registration.

Objective: To investigate the difference in registered comorbidities and complications between prospective and retrospective data collection in patients with bladder cancer undergoing radical cystectomy.

Method: Seventy-three bladder cancer patients undergoing radical cystectomy were randomized to receive prospective or retrospective collection of data regarding comorbidities and complications. Data in the prospective arm was collected daily during hospitalization, 14-days after discharge and 90-days postoperatively. In the retrospective arm, medical records were reviewed retrospectively at 90-days. Comorbidities were compared using the Charlson Comorbidity Index (CCI) and complications were reported as overall, minor and major dependent on Clavien Dindo Classification (CDC). The primary endpoint was the difference in overall complication rate.

Results: No statistically significant difference in CCI was observed with median [IQR] 2[0;3] and 1[0;2] ($p = 0.21$). No statistically significant difference was found regarding all, minor (CDC I-II) or major (CDC III-V) complications at all three time points.

Conclusion: No statistically significant difference in comorbidity and complications between retrospectively and prospectively collected data was observed. We find that retrospective collected data is reliable when strict reporting guidelines are used in this single-centre study.

ARTICLE HISTORY
Received 30 December 2020
Revised 20 September 2021
Accepted 28 September 2021

KEYWORDS
Retrospective; prospective; complications; comorbidities; bladder cancer; radical cystectomy; Clavien Dindo

Introduction

The quality and accuracy of retrospective versus prospective collection of data is a common source of disagreement between researchers [1]. Despite the general belief that prospectively collected data is more accurate than retrospectively collected data [2], most data for surgical studies assessing complication rates are collected retrospectively [3]. Clinical databases are based predominantly on data written in medical records transferred retrospectively to the database. Multiple problems with data collected retrospectively from medical records exist: (1) conflicting data, (2) missing data, and (3) medical records do not allow for correction of data [4]. Furthermore, it can pose a problem when the data is not collected with the exact registration or specified definitions of comorbidities and complications in mind. This can be a significant source of error. Finally, most complications that do not require major re-intervention, re-operation or readmission are likely to be under-reported [5].

In the present trial, we aimed to evaluate the difference in retrospective versus prospective collected data on comorbidities and complication rates after radical cystectomy in bladder cancer patients. We hypothesized that more minor complications would be registered if a strict prospective data collection was used compared to retrospective collection from medical records. The study was conducted at a hospital where a strict policy for reporting complications after urological surgery was already incorporated in the clinic.

Materials and methods

Design

The trial was a single-blinded, randomized controlled trial (RCT). The trial included consecutive patients who underwent

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Supplemental data for this article can be accessed here.

radical cystectomy and urinary diversion because of bladder cancer [6] at a single tertiary university hospital in Denmark between October 2016 and April 2017. Inclusion criteria were age >18 years, oral and written informed consent and planned radical cystectomy due to bladder cancer. Patients were excluded if they failed to undergo radical cystectomy. The patients were exposed to either standard collection of complication rates retrospectively through medical journals or prospectively through questionnaires and interviews. The primary endpoint was the difference in reported complication rate within 90 days when comparing prospectively and retrospectively collected data.

Secure web-based computer randomization using REDCap (Department of Clinical Medicine, Aarhus University) [7] was used to allocate patients into two different groups at a 1:1 ratio by permuted block randomization with random varying block sizes of 4, 6 and 8. The treating physicians were blinded to randomization and definitions of complications. Pre-operative comorbidities were graded with the Charlson Comorbidity Index (CCI) [8]. Complications were graded with Clavien-Dindo Classification of surgical complications (CDC) [9,10] that was pre-defined before enrolment (Table 1). Minor complications were defined as CDC grade 0, I and II, whereas major complications were defined as CDC grade III, IV and V. Reporting of comorbidities and complications was made in agreement with recommendations from the European Association of Urologists (EAU) guidelines (Supplementary Tables S1 and S2) [11]. In both groups, standard registrations were made in the electronical medical record as part of clinical routine. Complication rates were registered separately for three different time intervals; (1) in-hospital, defined as the period between the cystectomy and until discharge, (2) 14 days after discharge and (3) 90 days, defined as the interval from (2) up to 90 days posteroperatively. Secondary endpoints were: (1) difference in minor complications, (2) difference in major complications and (3) difference in comorbidities.

Retrospective data collection

Baseline data and data regarding preoperative comorbidity and postoperative complications were collected retrospectively from patient records 90 days after surgery on patients in the control arm (Figure 1).

Prospective data collection

Information on comorbidity and complications were collected through questionnaires and daily ward rounds. At the first postoperative day, the patient received two questionnaires; one regarding comorbidities and one aimed at prospective registration of complications from discharge until the first planned outpatient clinic appointment 14 days after discharge. The patients were instructed to answer the questionnaires regarding complications the day before their visit at the outpatient clinic. At the 14 days visit, the patients returned the first questionnaire on complications and received a new, identical questionnaire for registration of complications up to 90 days postoperatively (Figure 1). The questionnaires were developed for this specific trial having in mind the CDC. The questionnaire regarding comorbidities was primarily a binary questionnaire whereas the questionnaire regarding complications was made with the possibility of free text. The death status of the patients was looked up in the medical journals. Analysis of data in the prospective arm was performed blinded to any findings in the medical journal.

Ethical considerations

The trial was conducted in accordance with the Declaration of Helsinki. The trial was approved by the Danish Data Protection Agency and local ethics committee. Clinical Trial identifier: NCT03052504.

Statistical methods and data management

Statistical analysis was performed using STATA 13 for Windows. Continuous variables were presented as means with standard deviations if the data followed a normal distribution, and otherwise median with inter-quartile range. Distributions were checked using histogram and QQ-plots. The significance was tested with student's *t*-test if the data met the criteria for parametric data. If the data did not meet these criteria, a Wilcoxon Mann-Whitney test was used. Binary and categorical data were given as frequencies and tested using the chi-squared test.

The proportion of complications with retrospective collection was assumed to be 50% [12]. From our own internal prospective quality database, we estimated the complications rate when strict reporting guidelines and prospective collection was used to be 85%. An estimated dropout of 10%, a ratio of 1:1, a significance level of 0.05 and a power of 0.80 was assumed. To detect a difference in complication rates between the two collection methods, 73 patients were needed in the trial.

Results

Flowchart

Seventy-three patients were enrolled, 35 in the retrospective group and 38 in the prospective group. In the retrospective group two patients died. In the prospective group, one patient died, two patients were transferred to another hospital and one patient was lost to follow-up (Figure 1). High adherence to the questionnaire in the prospective arm was observed, with only one patient not returning the questionnaires.

Patient and operative characteristics

Baseline characteristics did not differ between the two groups except for age at surgery where patients in the retrospective group were older (72.6 ± 8.7) than in the prospective group (68.1 ± 8.5) ($p = 0.03$) (Table 2).

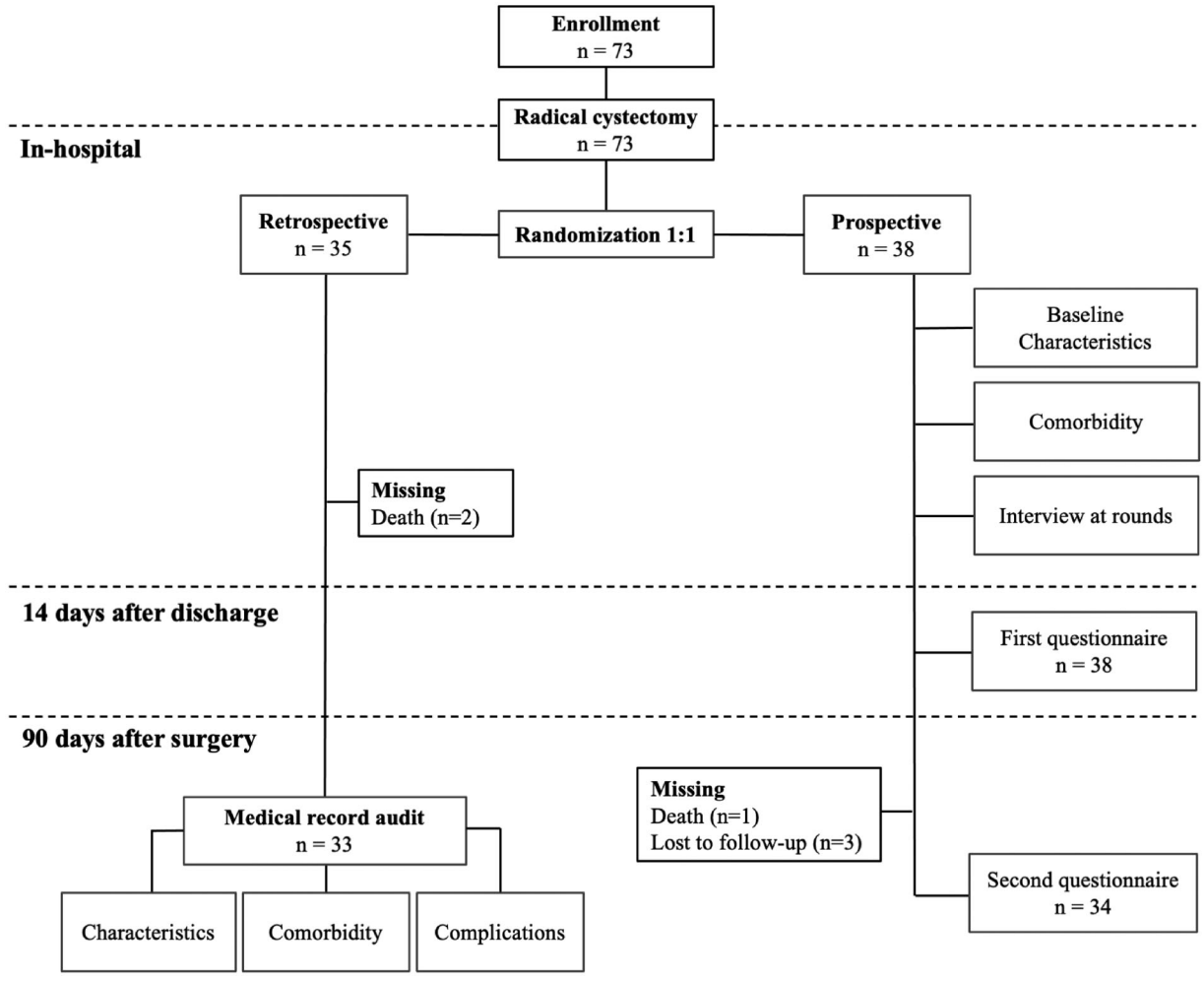

Figure 1. Flowchart of enrolment, randomization and follow-up. In the retrospective group, data was collected 90-days after randomization. In the prospective group, data were collected during in-hospital rounds, at 14 days after discharge and 90 days after surgery.

Pre-operative comorbidities

CCI were not significantly different in the two groups (Table 3). However, specific gastrointestinal and immunologic/rheumatic comorbidities were significantly different in the two groups.

Post-operative complications

No statistically significant difference was observed between groups for overall, minor and major complication rates. Minor in-hospital complications frequency was 71% and 77% ($p = 0.32$) for the prospective and the retrospective group, retrospectively. Fourteen days after discharge it was 58% and 46% ($p = 0.43$) and 90 days after surgery it was 32% and 18% ($p = 0.18$), respectively (Table 4). The total complication rates were primarily driven by gastrointestinal, haematological and infectious CDC 0, I and II (Supplementary Tables S3 and S4). The total number of complications are reported in Supplementary Table S5.

Discussion

Patients who are to undergo radical cystectomy are predominantly elderly with multiple comorbidities [13], furthermore radical cystectomy is associated with a high risk of complications in cancer surgery [14]. These patients' complications are therefore important to study because they may experience increased morbidity resulting in decreased quality-of-life. Also, complications that do not require re-intervention or re-operation are likely underreported unless they lead to readmission [5]. This is one of the potential reasons for an even distribution in the reporting of major complications requiring re-operation when comparing surgical case series, while the number of minor complications are much more variable [15,16]. Minor complications may, however, still have a major impact on a patient's quality-of-life and could potentially be prevented.

In the current trial, we found that in overall, major, and minor complications there was no significant difference in complication rates between the prospective and retrospective gathering of data. Nagurney et al. [2] found in an observational cohort a 28% mistranscription from patient to clinician. They concluded that 'Information obtained retrospectively from the abstraction of medical records is measurably less accurate than information obtained prospectively from research subjects'. This is in contrast to the present findings where no statistically significant difference was observed. Several reasons for this may exist; Mitropoulos et

Table 2. Baseline characteristics.

	Prospective ($n = 38$)	Retrospective ($n = 35$)	p-value
Gender (Male)	26 (68%)	25 (71%)	0.78
Age at surgery	68.1 ± 8.5	72.6 ± 8.7	0.03
Body mass index (kg/m^2)	27.0 ± 4.2	25.9 ± 3.6	0.22
Very obese (BMI > 30 kg/m^2)	9 (24%)	6 (17%)	0.49
Prior abdominal surgery	10 (26%)	7 (20%)	0.52
Prior nephroureterectomy	3 (8%)	2 (6%)	0.71
Previous systemic chemotherapy*	2 (5%)	1 (3%)	0.60
Previous radiotherapy*	5 (13%)	2 (6%)	0.28
Preoperative hydro nephrosis	9 (24%)	8 (23%)	0.93
Operating room time (in minutes)	317 [260; 361]	317 [265; 369]	0.94
Type of operation			
Primary Open surgery	23 (61%)	19 (54%)	0.59
Primary Robotic surgery	15 (40%)	16 (46%)	0.59
Converted	2 (5.2%)	1 (2.9%)	0.60
Estimated blood loss (ml) ($n = 54$)	1,100 [350; 2,135]	650 [300; 1,300]	0.11
Total PRBCs received	0 [0;1]	0 [0; 0]	0.53
Total number of FFP received	0 [0;0]	0 [0; 0]	0.56
Type of urinary diversion (Conduit)	36 (95%)	32 (91%)	0.56
Undergoing major operational intervention(s) other than the cystectomy, in the same operation.	0 (0%)	3 (9%)	0.07
Intraoperative surgical complications	1 (3%)	4 (11%)	0.14
ASA score	2 [2; 3]	2 [2; 3]	0.75
Abnormal preoperative creatinine level**	8 (21%)	13 (37%)	0.13
Lymph node dissection	37 (97%)	34 (97%)	0.95
Organ-confined disease (3 months postoperative)	30 (79%)	27 (77%)	0.85

n, the total number of patients within that category. Numbers are given as Mean ± SD/Median [IQR] or Frequency (%). *Not including this surgery. **>105 μmol/L for males, >90 μmol/L for females.

Table 1. Clavien-Dindo classification (CDC) of surgical complications.

CDC-Grade	Definitions
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Acceptable therapeutic regimens are: drugs such as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II	Requiring pharmacological treatment with drugs other than those allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anaesthesia
Grade IIIb	Intervention under general anaesthesia
Grade IV	Life-threatening complication (including CNS complications: brain haemorrhage, ischaemic stroke, subarachnoid bleeding, but excluding transient ischaemic attacks) requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multi-organ dysfunction
Grade V	Death of a patient

Table 3. Number of pre-operative comorbidities on individual patient level.

Pre-operative comorbidities, grouped	Prospective	Retrospective	p-value
Charlson Comorbidity Index	2 [0; 3]	1 [0; 2]	0.21
Cardiovascular	1 [1; 3]	1 [0; 2]	0.07
Pulmonary	0 [0; 0]	0 [0; 0]	0.10
Gastrointestinal	0 [0; 0]	0 [0; 0]	0.03
Neurological	0 [0; 0]	0 [0; 0]	0.09
Endocrine	0 [0; 0]	0 [0; 0]	0.88
Immunologic/rheumatic	0 [0; 0]	0 [0; 0]	0.01
Renal	0 [0; 0]	0 [0; 0]	0.58
Oncology	0 [0; 0]	0 [0; 0]	0.90
Other	0 [0; 0]	0 [0; 0]	0.34

Numbers are given as Median [IQR].

al. [17] states that definitions of surgical complications lack standardization and that if standardized reporting methodology were implemented in the field of urology, it would be easier to intreperet surgical performance. In the present trial, a standardized reporting methodology with clear definitions of complications and comorbidities was used when analysing questionnaires and medical journals. The large aligment in complication rates could be caused by the fact that a standardized reporting method has already been implemented at our institution. Gandaglia et al. [18] found, in a cohort study on comparison of prospective and retrospective collection of complications, a higher complication rate when collecting prospectively (29% versus 10% $p < 0.001$). This is in great contrast to the present trial where we did not see this difference but interestingly found a much higher complications rate at all three time points. Elmussareh et al. [19] showed that 92% (575/625) of patients experienced one or more complications following radical cystectomy when retrospective collection was used. Also, Shabsigh et al. [15] found a high complication rate of 64% (735/1,142). These complications rates are comparable to the present trial and may indicate that the true complication rate after radical cystectomy is significantly higher than what we have previously assumed. The strength of an RCT is to decrease the risk of residual confounding which was successful in the present study. However, a potential misclassification may exist by the fact that collection of the outcome (difference in reported complication rates) is associated to the exposure (collection of complications). This may lead to a differential misclassification. However, if this was the case we would expect to have lower complication rates than observed and possibly a difference favouring higher complication rates in the prospective arm. Moreover, our trial indicates that, if a strict registration protocol is used, retrospective data collection is reliable for comparison of complication rates.

Several methods for prospective collection of complication rates exists and some rely on more information from the patients themselves than others. In the present trial,

Table 4. Frequency of complications at individual patient level during follow-up.

	In hospital					14 Days					90 Days				
Complications	Prospective		Retrospective		*p*-value	Prospective		Retrospective		*p*-value	Prospective		Retrospective		*p*-value
All (CDC 0-V)	27	71%	27	77%	0.32	23	61%	20	57%	0.95	13	38%	10	30%	0.49
Minor (CDC 0, I & II)	27	71%	27	77%	0.32	22	58%	16	46%	0.43	11	32%	6	18%	0.18
Major (CDC III, IV & V)	5	13%	7	20%	0.37	12	31%	11	31%	0.88	6	18%	6	18%	0.95

CDC, Clavian-Dindo classification. Left column is the number of patients with one or more complications and the right column is the frequency of patients with one or more complications.

patient-reported outcomes (PRO) were chosen as supplementary to observed data. However, the observer performed minor interpretations of the questionnaire in order to grade complications regarding CDC. PRO data gives the observer the possibility to observe subjective and less severe symptoms and complications [20] than directly reported to the physician. In this case, PRO was constructed as a questionnaire and therefore a strict systematic approach to reporting of complications was obtained. Especially when minor complications are encountered these are often overseen by the hospital staff or not put into the medical records. The present study shows that when a strict reporting guideline at the out-patient clinic is used, PRO data is directly comparable to medical records, even on minor complications.

Limitations

The questionnaire was not validated prior to the trial and this potentially may lead to a differential misclassification since there is a risk that patients in the prospective arm may misinterpret the questionnaire which may lead to over- or under-estimation of the complication rate. When using strict definitions in both groups we tried to make any differential misclassification more non-differential. Moreover, the trial is under-powered to look at subgroups. Most importantly, the findings are most likely only transferable to institutions with detailed medical records who follow the EAU recommendations on complication registration.

Conclusion

The present randomized controlled trial found no statistically significant difference regarding registered comorbidity and complications after radical cystectomy, whether these were collected retrospectively or prospectively, in this single centre RCT. Our findings underline the need for a strict protocol for detecting complications after radical cystectomy. More studies are needed in order to investigate how to implement and optimize complication-reporting guidelines in different clinical settings.

Acknowledgments

Thanks to Rikke Nygaard Knudsen, Anna Munk Nielsen and Anna Krarup Keller for helping this trial along and thanks to Jakob Hjort for helping with data management.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The Department of Nephrology Aarhus University Hospital Denmark, Dagmar Marshalls Fund and Inge Eriksens Foundation supported the work.

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