ORIGINAL ARTICLE

Surgical site infections in patients who undergo radical cystectomy: Excess mortality, stay prolongation and hospital cost overruns

E. Gili-Ortiz\textsuperscript{a,*}, R. González-Guerrero\textsuperscript{a}, L. Béjar-Prado\textsuperscript{b}, J. López-Méndez\textsuperscript{b,c}, G. Ramírez-Ramírez\textsuperscript{b,c}

\textsuperscript{a} Servicio de Anestesiología y Bloque Quirúrgico, Hospital Universitario Virgen Macarena, Sevilla, Spain
\textsuperscript{b} Departamento de Medicina Preventiva y Salud Pública, Facultad de Medicina, Universidad de Sevilla, Sevilla, Spain
\textsuperscript{c} Servicio de Medicina Preventiva y Salud Pública, Hospital Universitario Virgen Macarena, Sevilla, Spain

Received 29 September 2014; accepted 3 November 2014
Available online 1 April 2015

KEYWORDS
Radical cystectomy; Surgical site infection; Mortality; Hospital stay; Costs

Abstract

Background: The aim of this study was to analyze the impact of surgical site infections (SSI) in patients who underwent radical cystectomy, in terms of excess hospital mortality, stay prolongation and cost overruns.

Material and methods: A retrospective observational study was conducted on a sample of patients who underwent radical cystectomy as recorded in the basic minimum data sets of 87 Spanish hospitals from 2008 to 2010.

Results: We studied 4377 patients who underwent radical cystectomy (3904 men and 473 women) of whom 849 (19.4\%) experienced a SSI. The patients with SSI were predominantly men, elderly and had a higher prevalence of alcohol-related disorders and more number of comorbidities. The patients with SSI had significant excess mortality (125.6\%), undue stay prolongation (17.8 days) and cost overruns (14,875.70 euros).

Conclusions: After controlling for demographic variables, hospital type, addiction disorders and comorbidities using multivariate pairing, the onset of SSI in patients who underwent radical cystectomy significantly increased the mortality, stay and cost. Certain preventive measures already established in previous studies could reduce the incidence of SSI and its healthcare and financial impact.

© 2015 AEU. Published by Elsevier España, S.L.U. All rights reserved.

\textsuperscript{*} Please cite this article as: Gili-Ortiz E, González-Guerrero R, Béjar-Prado L, López-Méndez J, Ramírez-Ramírez G. Infecciones de localización quirúrgica en los pacientes tratados con cistectomía radical: exceso de mortalidad, prolongación de estancias y sobrecostes hospitalarios. Actas Urol Esp. 2015;39:210-216.
\textsuperscript{*} Corresponding author.
\textit{E-mail address: egiliort@gmail.com} (E. Gili-Ortiz).

2173-5786/© 2015 AEU. Published by Elsevier España, S.L.U. All rights reserved.
PALABRAS CLAVE
Cistectomía radical; Infección de localización quirúrgica; Mortalidad; Estancia hospitalaria; Costes

Infecciones de localización quirúrgica en los pacientes tratados con cistectomía radical: exceso de mortalidad, prolongación de estancias y sobrecostes hospitalarios

Resumen

Introducción: El objetivo de este estudio es el análisis del impacto de las infecciones de localización quirúrgica (ILQ) en los pacientes tratados con cistectomía radical, en términos de exceso de mortalidad intrahospitalaria, prolongación de estancias y sobrecostes.

Material y métodos: Estudio observacional retrospectivo de una muestra de pacientes tratados con cistectomía radical recogidos en los conjuntos mínimos básicos de datos de 87 hospitales españoles durante el periodo 2008-2010.

Resultados: Se estudió a 4.377 pacientes tratados con cistectomía radical, 3.904 varones y 473 mujeres, de los cuales 849 (19.4%) experimentaron una ILQ. Los pacientes con ILQ fueron predominantemente varones, de mayor edad, con mayor prevalencia de trastornos asociados al consumo de alcohol y con más comorbididades. Los pacientes con ILQ presentaron importantes excesos de mortalidad (125,6%), prolongación indebida de estancias (17,8 días) y sobrecostes (14.875,7 euros).

Conclusiones: Controlando mediante el emparejamiento multivariado las variables demográficas, el tipo de hospital, los trastornos adictivos y las comorbididades, la aparición de ILQ en pacientes tratados con cistectomía radical aumenta significativamente la mortalidad, la duración de la estancia y su coste. Ciertas medidas preventivas ya consagradas en estudios previos podrían disminuir su incidencia y su impacto sanitario y económico.

© 2015 AEU. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Introduction

Radical cystectomy (RC) may have a high rate of postoperative complications and, according to various studies, it appears in 20–64% of operated patients, resulting in a in-hospital mortality of 2–6%. Complications of RC may cause excess mortality, undue prolongation of hospital stays, and significant overruns.

One of the most common complications of RC is infection of the surgical wound, generically called surgical site infection (SSI), which usually worsens the prognosis, prolongs hospital stay and, in some cases, produces unscheduled readmissions. Despite the importance of this complication, we could not find any publication that has analyzed the impact of these infections in these patients in Spain in terms of attributable mortality, lengthening of stays, and excess costs.

Therefore, we studied this problem in 18-year-old patients or older admitted to a sample of 87 Spanish hospitals during the period 2008–2010, trying to control other confounding and interaction variables such as age, sex, type of hospital, addictions, and comorbidities. The aim of this study is to analyze the possible influence of these infections on mortality, longer stays, and excess costs among hospitalized patients undergoing RC.

Material and methods

Type of study, sample and participants

Retrospective observational study in a sample of Spanish hospitals.

For the sample to have national and regional representation, and taking into account the stratification of hospitals as rated by hospital groups according to their size and complexity of the Ministry of Health, Social Services, and Equality's multistage sampling was conducted in which 87 Spanish hospitals of all Spanish Autonomous Communities were selected.

From the written or digitized medical history information, the diagnoses of each patient and the procedures that are applied are encoded according to the rules of the 9th Revision of the International Classification of Diseases and Causes of Death (ICD9). The coding and entering of information in the database are carried out by specialized data logging personnel. These databases contain demographic information, dates of admission and discharge, type of admission, type of discharge, diagnostic codes for the primary cause and secondary diagnoses, external causes and procedures, using the ICD9 codes, and they are called basic minimum data set (BMDS). In these databases, diagnosis-related groups (DRGs) are also included and each hospital is ranked in a group according to their size and care complexity. The analysis was restricted to patients that at the time of discharge were 18 or more.

Variables

We defined as cases of RC those with procedure code 57.71 of the ICD9 diagnosed with bladder cancer (ICD9 codes 188.0-188.9). Age was measured in years. As an indicator of comorbidity, the Charlson comorbidity index was calculated using the ICD9 codes proposed by Quan et al. for the comorbidities of this index. Other comorbidities that were analyzed were also calculated using the codes proposed by
Quan et al. The ICD9 codes were used to define disorders due to alcohol, tobacco, and other addictions.

Hospitals were divided into 5 groups according to the classification of the Ministry of Health, Social Services, and Equality by size and care complexity, essential for the control of confounding bias and for calculating healthcare costs. The distinguishing characteristics of each group are presented in Appendix A.

We applied the criteria of Wit et al. to identify patients with SSI (ICD9 codes 998.31-998.32, 998.51, 998.59 and 998.83). In order to distinguish patients admitted with these infections from those who acquired them after cystectomy, all cases in which the codes of these infections appeared in the primary diagnosis were excluded. Patients with less than two-day stays and those whose reason for discharge was the transfer to another facility were also excluded from the analysis.

Data analysis

The main objective was to determine the mortality, length of stay, and hospital costs in patients treated with RC with and without these infectious complications. We calculated the costs at discharge from hospital-specific costs for each DRG, stratified by hospital group, using the estimates published by the Ministry of Health for the years 2008-2010.

A bivariate analysis was carried out to examine the relationship between SSI and age, sex, addictive disorders, comorbidities, and Charlson index, using the chi-square test (or its non-parametric variants) and Student’s t-test (or its non-parametric variants). The hazard ratio for mortality from SSI was calculated by dividing the incidence of mortality among patients with SSI and the incidence of mortality among those without SSI.

To minimize the risk of confounding bias we did a multivariate matching of patients with RC and SSI to patients with RC without SSI using propensity scores calculated by logistic regression analysis. The cases and no cases of SSI were paired in the multivariate model by age group, sex, hospital group, alcohol consumption disorders, tobacco consumption disorders, and Charlson comorbidity index. Each case of SSI was matched at least to 4 no cases. The extension of stays, overruns, and excess mortality attributable to SSIs were obtained by subtracting the means of cases from the means of the unpaired no cases.

The analysis was carried out with the statistical program STATA version MP 13.1.

Results

Characteristics of patients

The characteristics of the patients treated with RC with SSI and without are shown in Table 1. A total of 4377 patients treated with RC were identified, 3904 men and 473 women, of which 849 (19.4%) had a SSI during their stay in hospital. Patients with SSI were older (mean age 67.1 years), predominantly male (91.6%), and with higher prevalence of disorders associated with alcohol consumption (8.0%). They also had higher prevalence in some of the comorbidities studied such as electrolyte imbalance, weight loss, congestive heart failure, and chronic renal disease. The prevalence of SSI was slightly higher in type-2 (20.9%) and type-4 (21.2%) hospitals, but the differences were statistically significant.

The distribution by age and sex groups of patients treated with RC of the sample is exposed in Fig. 1.

Figure 1  Distribution of cases of radical cystectomy of the sample by age and sex groups.

Mortality

The mortality rate among patients with RC who had a SSI was 10.2% (Table 1) and that of those without SSI 4.2% (hazard ratio: 2.5; 95% LC: 1.9–3.2; p < 0.0001). Mortality among patients with RC and SSI was higher in type-2 (13.8%) and type-5 (11.1%) hospitals, but the differences were not statistically significant.

Fig. 2 shows the distribution by age and sex groups of deaths that occurred during the hospital stay among patients treated with RC.

The characteristics of patients treated with RC who died and did not die during their hospital stay are shown in Table 2. Deceased patients were older (mean age 71.0 years) and mostly male (88.9%). The deceased had higher prevalence in some of the studied comorbidities such as obesity, cardiac arrhythmias, disorders of the pulmonary circulation,
valvular heart disease, electrolyte imbalances, coagulation disorders, cerebrovascular disease, congestive heart failure, liver disease, diabetes with complications, and chronic renal disease. As a result, the Charlson comorbidity index was higher among those who died (4.5 versus 3.8). The incidence of SSI was significantly higher among patients treated with RC who died during their hospital stay (37.2 versus 18.4%).

**Attributable extension of stays, overruns and excess mortality**

Table 3 shows the results of the comparative analysis of cases of SSI with unpaired SSI no cases. All cases of SSI were paired with at least 4 no cases. Undue prolongation of hospital stays among patients with RC and SSI was on average 17.8 days, the overruns for discharge among those with RC and SSI were on average 14,875.7 euros, and excess mortality attributable to SSIs among these cystectomized patients was 125.6%.

**Discussion**

Our results indicate that SSIs, in addition to the other factors analyzed, have a considerable impact on hospital mortality of patients treated with RC, with excess mortality attributable to these infections of 125.6%. According to the analysis results, mortality may be influenced by a higher incidence of SSIs, in addition to the other factors mentioned above which have been included in the models. Also, these postoperative infections caused significant extensions...
of hospital stay (17.8 days) and overruns due to discharge (14,875.7 euros) in these patients.

Thanks to the sample size and the diversity of hospitals, these results are generalizable and are not limited to patients admitted to one or a few hospitals. To our knowledge, this is the first study in Spain which calculates excess mortality, longer stays, and excess of costs attributable to SSIs in patients who have been treated with a RC, controlling a large number of variables present at admission.

Proper control of the confounding bias is the main challenge that those trying to analyze the impact of the different surgical complications on the prognosis and other outcomes of patients face, using large healthcare databases. The stays, costs, and in-hospital mortality differ depending on reason for admission, severity of the disease, accompanying comorbidities, type of hospital, and other demographic and social characteristics of patients. Including the group of hospitals in the model to control the confounding bias is very important because the scientific evidence points to differences in the quality of urological cancer surgery depending on the type and the equipment of the center. The procedure of multivariate matching by propensity scores makes it possible to evaluate the effects in observational studies in which there has been no randomization like in randomized clinical trials. The results of other studies which have used similar methodologies analyzing large databases of healthcare data indicate that a pairing relationship 1:4 is valid and reliable.

Our study has several limitations. The data we used are exclusively those contained in the BMDS, and they were not supplemented with additional patient data. For example, we do not know in which patients a suitable antimicrobial prophylaxis was performed or if the list of surgical safety was correctly applied. Throughout the study we have used

### Table 2 Characteristics of deceased patients treated with cystectomy and no deaths during hospitalization.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Deaths (n = 234)</th>
<th>No deaths (n = 4143)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>26 (11.1)</td>
<td>447 (10.8)</td>
<td>0.519&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Men</td>
<td>208 (88.9)</td>
<td>3126 (89.2)</td>
<td>0.519&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Age (years), mean (95% CI)</strong></td>
<td>71.0 (70.0–72.0)</td>
<td>66.1 (65.8–66.4)</td>
<td>&lt;0.0001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Alcohol disorder</td>
<td>21 (9.0)</td>
<td>263 (6.3)</td>
<td>0.1126&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Tobacco disorder</td>
<td>80 (34.1)</td>
<td>1727 (41.7)</td>
<td>0.0234&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Other drugs disorder</td>
<td>2 (0.9)</td>
<td>34 (0.8)</td>
<td>0.9553&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>14 (6.0)</td>
<td>141 (3.4)</td>
<td>0.0378&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Uncomplicated hipertensión</td>
<td>67 (28.6)</td>
<td>1334 (32.2)</td>
<td>0.2552&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hypertension with complications</td>
<td>12 (5.1)</td>
<td>150 (3.6)</td>
<td>0.2346&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
<td>39 (16.7)</td>
<td>273 (6.6)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Disorders of pulmonary circulation</td>
<td>5 (2.1)</td>
<td>21 (0.5)</td>
<td>0.0016&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>7 (3.0)</td>
<td>57 (1.4)</td>
<td>0.0452&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Deficiency anemia</td>
<td>1 (0.4)</td>
<td>31 (0.7)</td>
<td>0.5751&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Posthemorrhagic anemia</td>
<td>3 (1.3)</td>
<td>24 (0.6)</td>
<td>0.1816&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Electrolyte imbalance</td>
<td>25 (10.7)</td>
<td>58 (1.4)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Weight loss</td>
<td>8 (3.4)</td>
<td>164 (4.0)</td>
<td>0.6793&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>3 (1.3)</td>
<td>44 (1.1)</td>
<td>0.7507&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>16 (6.8)</td>
<td>43 (1.0)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>10 (4.3)</td>
<td>123 (3.0)</td>
<td>0.2580&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>14 (6.0)</td>
<td>77 (1.9)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>cerebrovascular disease</td>
<td>7 (3.0)</td>
<td>43 (1.0)</td>
<td>0.0062&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dementia</td>
<td>1 (0.4)</td>
<td>6 (0.1)</td>
<td>0.2927&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>31 (13.2)</td>
<td>555 (13.4)</td>
<td>0.9483&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Rheumatic disease</td>
<td>3 (1.3)</td>
<td>30 (0.7)</td>
<td>0.3371&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>2 (0.9)</td>
<td>46 (1.1)</td>
<td>0.7149&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mild liver disease</td>
<td>6 (2.6)</td>
<td>40 (1.0)</td>
<td>0.0196&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetes without chronic complications</td>
<td>40 (17.1)</td>
<td>637 (15.4)</td>
<td>0.4793&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetes with chronic complications</td>
<td>9 (3.8)</td>
<td>29 (0.7)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Renal disease</td>
<td>31 (13.2)</td>
<td>75 (1.8)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Moderate or severe liver disease</td>
<td>7 (3.0)</td>
<td>10 (0.2)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Metastatic cancer</td>
<td>67 (28.6)</td>
<td>994 (24.0)</td>
<td>0.1071&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Charlson index, mean (95% CI)</td>
<td>4.5 (4.1–4.9)</td>
<td>3.8 (3.7–3.9)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Surgical site infection</td>
<td>87 (37.2)</td>
<td>762 (18.4)</td>
<td>&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Test: Chi-square.
<sup>b</sup> Test: Student’s t.
Surgical site infections in patients who undergo radical cystectomy

Table 3  Undue prolongation of hospital stays, overruns, and excess mortality attributable to surgical site infections in patients treated with radical cystectomy.

<table>
<thead>
<tr>
<th></th>
<th>Adjusted mean of patients cystectomized with SSI</th>
<th>Adjusted means of patients cystectomized without SSI</th>
<th>Difference of means</th>
<th>95% CI margin of the difference</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolongation of hospital stays due to SSI (days)</td>
<td>37.4</td>
<td>19.6</td>
<td>17.8</td>
<td>15.7–19.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Overruns attributable to SSI (euros)</td>
<td>33,533.4</td>
<td>18,657.7</td>
<td>14,875.7</td>
<td>12,782.9–16,968.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Difference of mortality rates and excess mortality attributable to SSI (%)</td>
<td>9.54</td>
<td>4.23</td>
<td>5.31 (excess mortality: 125.6)</td>
<td>3.49–7.39 (excess mortality: 92.8–149.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

SSI: surgical site infections.

the definitions of addictive disorders, of the comorbidities, and of the SSI as they were assigned by physicians in each center, and then coded and entered into the database by coders, without knowing the possible variability among different centers. The ICD9 codes to identify SSIs are those used internationally for studies that exploit databases of hospital discharges, but these codes are not designed to measure the different types of SSI with the precision that the criteria recommended by the Centers for Disease Control of the U.S.A. stipulate, which may cause an underestimate of the true incidence. However, a recent meta-analysis found that the sensitivity and specificity of SSI diagnoses from healthcare databases are satisfactory, and better than that of the diagnoses of other infections associated with healthcare.

Databases such as the BMDS also have significant advantages. The data collected are usually completed in almost all discharges and, by including all cases, they provide fairly accurate estimates of incidence, prevalence, comorbidities, complications, and mortality of diseases treated in hospitals. These data can be analyzed retrospectively, unlike other designs that require a prospective data collection. The cost data due to DRG stratified by groups of hospitals that are updated annually extremely facilitate the cost and overrun analysis, and an invaluable additional advantage to BMDS is added. Data collection for long periods and with a large number of patients, as in this study, can be done relatively quickly and easily, and since data are systematically collected, the reduction of efforts and cost is considerable. In these studies, there may be fewer selection biases, as the rejection of the patients or their legal representatives to sign the consent and participate in the study.

From the results, a number of preventive measures can be inferred, including not only those aimed at the importance of following safety measures and proper surgical technique, and prevention of infections, but also other very important ones in the preoperative period like weight management and nutritional status of the patient, and abstinence from tobacco, alcohol, and other drugs by brief advice or referring them to detoxification centers if necessary. Despite the standardization of surgical techniques and improvements in anesthetic protocols and perioperative care, morbimortality subsequent to RC is still very high, so new protocols and promising guidelines of enhanced recovery after surgery or ERAS specific to RC are being increasingly used.

We believe that all these measures would help reduce the risk of SSI and excess mortality, undue prolongation of stays and overruns that this complication produces in patients treated with RC, as well as avoid or reduce their personal and family suffering.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

This study was funded by Grants for Funding of Biomedical Research and Health Sciences in Andalusia for 2013 by the Ministry of Health and Social Affairs of the Government of Andalusia (PI-0271-2013) and the Government Delegation for the National Plan on Drugs (Help 2009I017, Project G4I825811).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.acuroe.2015.03.003.

References