The Cost of Postoperative Complications and Economic Validation of the Comprehensive Complication Index

Prospective Study

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Objective: To validate the Comprehensive Complication Index (CCI) via an assessment of its relation to postoperative costs.

Background: The CCI summarizes all the postoperative complications graded by the Clavien-Dindo classification (CDC) on a numerical scale. Its relation to hospital costs has not been validated to date.

Methods: Prospective observational cohort study, including all patients undergoing surgery at a general surgery service during the 1-year study period. All complications graded with the CDC and CCI and related to the initial admission, or until discharge if the patient was readmitted within 90 days of surgery, were included. The surgeries were classified according to their Operative Severity Score (OSS) and in 4 groups of homogeneous surgeries. All postoperative costs were recorded.

Results: In all, 1850 patients were included, of whom 513 presented complications (27.7%). The CDC and the CCI were moderately to strongly correlated with overall postoperative costs (OPCs) in all OSS groups (r_s = 0.444–0.810 vs 0.445–0.820; $P < 0.001$), homogeneous surgeries (r_s = 0.364–0.802 vs 0.364–0.813; $P < 0.001$), prolongation of postoperative stay ($r_s = 0.802$ vs 0.830; $P < 0.001$), and initial operating room costs ($r_s = 0.448$ vs 0.451; $P < 0.001$). This correlation was higher in emergency surgery. With higher CDC grades, the OPC tended to increase an upward trend. In the multivariate analysis, CDC, CCI, age, and duration of surgery were all associated with OPC ($P < 0.001$).

Conclusions: In our environment, the CCI presented associations with OPC. This demonstration of its economic validity enhances its clinical validity.

Keywords: Clavien-Dindo classification, Comprehensive Complication Index, costs and cost analysis, morbidity, postoperative complications, validation studies

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Although the costs associated with surgical complications are known to be high, there is little good-quality evidence of their real economic impact. Previous reports in the literature have only rarely used systems for classifying the severity of complications and their relation to economic costs, and the quantification and communication of the costs and resource use associated with postoperative morbidity are insufficient.[1]

The Clavien-Dindo classification (CDC) is the most frequently used system today for assessing postoperative morbidity.[2] The new Comprehensive Complication Index (CCI) summarizes all the results classified by the CDC on a numerical scale.[3] Recently, the CCI was clinically validated in all the surgical interventions performed at a General Surgery service[4,5]: the scale represented a slight improvement on the CDC in terms of its association with clinical results, and clearly outperformed the CDC in terms of the information provided in patients with 2 or more complications.

Although previous studies have assessed the costs of postoperative complications in various procedures classified using the CDC,[6–10] to locate any previous reports of an economic validation of the CCI, an unlimited PubMed search was conducted, updated on November 1, 2018, using the following strategy: ''Comprehensive Complication Index''. The full texts of 98 articles, 2 letters to the editor, and 1 editorial found were analyzed. Only 2 articles referred to the relationship between CCI and costs.[11,12]

Here, from the perspective of a hospital management service, we present an economic evaluation of the postoperative complications of all surgical procedures carried out at a General Surgery Service, and associate it with the data provided by the CDC and the CCI.

METHODS

This prospective observational cohort study had the following endpoints:

1. Primary endpoint: From the economic point of view, to validate the CDC and the CCI by analyzing their relationship with postoperative hospital costs. The variables considered for the analysis were the overall series, specific surgeries, surgeries classified according to their complexity, emergency or nonemergency, or the number of complications, and prolongation of the postoperative stay (defined later).
2. Secondary endpoints: To measure postoperative costs in all patients undergoing surgery at a general and digestive surgery service and to analyze the association of the operating room costs with the CDC and the CCI. Also, to determine the impact on the overall postoperative costs (OPCs) of the increase of one grade or point on the CDC and CCI in the different surgery groups.
3. Recruitment: All patients in a reference area of 254,609 inhabitants undergoing surgery during the 1-year study period (March 1, 2016 to February 28, 2017) were included. Patients undergoing minor outpatient surgeries such as removal of epidermal cysts, small lipomas, ingrowing toenails, and so on were excluded. The exclusion criteria are presented in Supplemental Digital Content 1

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(http://links.lww.com/SLA/B631). Patients who died were excluded from the calculation of the costs. The study was carried out at the public referral hospital in our geographical area.
4. Follow-up: We recorded all postoperative complications and their costs during the admission for the initial surgery, or until the patient was discharged after any additional admission occurring within 90 days as a result of complications. Complications and readmissions directly or indirectly associated with the hospital admission were included.

Analytical Methods Used to Test the Hypothesis

Calculation of Complications

To avoid subjective interpretations, and following the studies by Clavien et al,[2,13,14] a surgical complication was considered as any negative event occurring in a patient during hospitalization or within 90 days of surgery (or, if the hospitalization lasted longer than 90 days, until discharge), even if the event was only remotely related to the procedure.

All postoperative complications according to the CDC[2] were recorded, including asymptomatic complications.

The methodology used to compile and record the complications has been described elsewhere.[4] Briefly, before the start of the study, physicians were trained to record and grade all postoperative complications. Supporting documentation was used.[2,14–16] Any doubts were clarified in a clinical session. A form for reporting complications in the electronic medical record was created. Finally, the researchers consulted all the daily medical and nursing progress reports in the electronic medical record and in the form just mentioned.[4]

The CCI was calculated according to the formula described by the authors.[3] The CDC grades were grouped into 2 new categories:

1. CDC V1: No complications (grade 0), minor complications (grades I and II), and major complications (grades IIIa, IIIb, IVa, IVb).
2. CDC V2: A modified version of the original CDC, which combined grades IVa and IVb together because of the low number of cases in these categories.

Groups of Surgeries

Given the heterogeneity of the sample, Copeland et al's[17] Operative Severity Score (OSS) was used to classify all the initial surgical procedures into 4 groups according to their complexity: minor, moderate, major, and major+. The most frequent examples in each group were, respectively, hernioplasty, cholecystectomy, colectomy, and hepatectomy. The procedures included in each group in this series have been listed elsewhere[4] (Supplemental Digital Content 2, http://links.lww.com/SLA/B631). In addition, 4 groups of homogeneous surgeries were also analysed, which are listed below:

1. Appendectomy: Open and laparoscopic approach.
2. Colectomy: Open or laparoscopic, excluding low anterior resection of the rectum and abdominoperineal amputation. Emergency procedures were excluded.
3. Hernioplasty with admission.
4. Nonurgent laparoscopic cholecystectomy.

Prolonged Postoperative Stay

Hospital stay was considered to be prolonged if the patient was hospitalized for more than the 75th percentile for the surgical group in question.[18–20] In this calculation, deceased patients and those undergoing Day Surgery procedures were excluded.

Calculation of Costs

The economic analysis was carried out from the perspective of the hospital, so only direct hospital costs were taken into account. The costs attributed to each patient were provided by the Hospital's Economic Management Service. The costs were divided into: operating room costs (mean cost per minute of use), radiological examinations, and mean costs produced in the emergency department, the ward and/or intensive care unit (ICU) (services, structure, staff, functioning): the costs of medication, prosthesis, and care were mean costs and were not individualized for specific patients. For each patient, these data were used to calculate: initial operating room costs, all OPCs, reoperation costs, readmission costs, including those generated in the emergency department, and their corresponding examinations. All costs associated with preoperative tests, examinations or hospitalization, costs due to hospital admissions unrelated to complications of the index surgical procedure, and costs of the pathology study of the resected specimens were excluded.

The study sample comprises patients who underwent their initial surgery in the period between March 1, 2016 and February 28, 2017, and the complications were followed up until 90 days after surgery. Therefore, to avoid bias, 2016 prices were maintained in the costs charged in 2017.

Deceased patients were excluded from the calculation of costs, because the CCI in these cases is always 100 and the cost may be 0 if the patient dies in the operating room (a phenomenon known as nonsurvivor bias).[6,15]

The definitions of the variables used are shown in Supplemental Digital Content 3 (http://links.lww.com/SLA/B631), and the noneconomic data are compiled in Supplemental Digital Content 4 (http://links.lww.com/SLA/B631).

The project was approved by our hospital's Research Ethics Committee. Informed consent was not considered necessary. Patient data were anonymized before analysis.

Statistical Analysis

As the Shapiro-Wilk test confirmed that none of the costs analysed were normally distributed, nonparametric tests were used. Specifically, to compare the costs in 2 different groups of patients defined by 1 of the clinical variables, we used the Mann-Whitney *U* test and the Kruskal Wallis test if the comparison was to include more than 2 groups. In addition, if the classification variable was ordinal, the analysis was completed with a trend contrast, using the Cuzick test, to establish whether the costs increased with higher categories of the classification variable. Finally, if the comparison involved a quantitative variable, a nonparametric correlation coefficient (Spearman rank-correlation coefficient) was used. The correlation was considered weak ($r_s = 0.10–0.29$), moderate ($r_s = 0.30–0.49$), and strong ($r_s = 0.50–1.00$).[13,20]

Finally, to calculate the means adjusted for severity and groups, generalized linear models were used. Linear regression models were used to assess the effect of a 1-unit increase in the instruments analysed on the patient's overall costs (crude models).

After creating the crude regression models, we performed multivariate models adjusting the previous ones for potential independent factors. The statistical analysis is described in detail in the supplemental materials (Supplemental Digital Content 5, http://links.lww.com/SLA/B631). The statistical analysis was performed with Stata/SE v.12.0 and a P value <0.05 was considered statistically significant.

RESULTS

The group included in the final analysis comprised 1850 patients and 2111 surgical interventions. Ninety-six patients were excluded. No patients were lost to follow-up.

TABLE 1. Characteristics of the Total Series

Variables	All patients (N = 1850)	Operative Severity Score			
		Minor (n = 777)	Moderate (n = 625)	Major (n = 392)	Major+ (n = 56)
Age (y)†	57.12 (42.48–71.24)	54.11 (41.60–67.78)	53.27 (35.71–69.05)	66.58 (55.37–78.32)	68.07 (57.03–76.68)
Sex, male/female (%)	1112/738 (60.11/39.89)	560/217 (72.07/27.93)	314/311 (50.24/49.76)	204/188 (52.04/47.96)	52.04/47.96 (60.71/39.29)
ASA score (%)					
I	579 (31.29)	293 (37.71)	239 (38.24)	41 (10.46)	6 (10.71)
II	900 (48.64)	369 (47.49)	297 (47.52)	205 (52.30)	29 (51.79)
III	335 (18.10)	110 (14.16)	85 (13.60)	120 (30.61)	20 (35.71)
IV	33 (1.78)	5 (0.64)	4 (0.64)	23 (5.87)	1 (1.79)
V	3 (0.16)	0	0	3 (0.77)	0
Programming of surgery (%)					
Scheduled with admission	852 (46.05)	209 (26.90)	321 (51.36)	270 (68.88)	52 (92.86)
Emergency	590 (31.89)	176 (22.65)	288 (46.08)	122 (31.12)	4 (7.14)
Scheduled day surgery	408 (22.05)	392 (50.45)	16 (2.56)	0	0
Approach					
Conventional	1349 (72.91)	777 (100)	241 (38.56)	285 (72.70)	46 (82.14)
Laparoscopic	460 (24.86)	0	356 (56.96)	99 (25.26)	5 (8.93)
Converted	41 (2.21)	0	28 (4.48)	8 (2.04)	5 (8.93)
Surgery time (min)*	84.56 (73.98)	39.72 (20.63)	77.67 (43.13)	159.60 (78.65)	258.20 (114.53)
Mortality (%)	42 (2.27)	4 (0.51)	7 (1.12)	24 (6.12)	7 (12.5)
Morbidity (%)	513 (27.73)	83 (10.68)	141 (22.56)	249 (63.52)	40 (71.43)
Complications (%)					
No complication	1337 (72.27)	694 (89.32)	484 (77.44)	143 (36.48)	16 (28.57)
1 complication	249 (13.45)	61 (7.85)	80 (12.8)	100 (25.51)	8 (14.29)
More than 1	252 (13.62)	10 (2.82)	61 (9.76)	149 (38.03)	32 (57.16)
Length of hospital stay (d)†	2.00 (1.00–6.00)	0.00 (0.00–1.00)	2.00 (1.00–4.00)	7.00 (5.00–14.50)	13.00 (7.00–17.50)

*All results in mean and standard deviation.
†All results in median and interquartile range.
ASA indicates American Society of Anesthesiologists.

The characteristics of the patients and the series are displayed in Table 1. In all, 513 patients (27.7%) presented complications, and 42 (2.3%) died. The classification of the surgical procedures according to the OSS is shown in Supplemental Digital Content 2 (http://links.lww.com/SLA/B631). The classification of the different Scheduled Day Surgery procedures in the present study according to the Operative Severity Score is described in Supplemental Digital Content 6 (http://links.lww.com/SLA/B631).

The relations of the CDC and the CCI with the different variables are shown below.

OPC in the Total Series

The CDC and the CCI were strongly correlated with the OPC in the total series (r_s = 0.658 vs 0.661, respectively; $P < 0.001$) (Table 2). In addition, an upward trend ($P < 0.001$) was observed in the OPC with increasing CDC grades (Supplemental Digital Content 7, http://links.lww.com/SLA/B631).

OPC in the Homogeneous Surgical Groups

In the surgical groups, an upward trend ($P < 0.001$) in the OPC was observed with higher CDC grades ($P < 0.001$). For example, the median OPC associated with colectomy ranged from €2650.77 [interquartile range (IQR) 1962.96–3153.81] with CDC grade I to €54087.74 (IQR 4018.50–104156.98) with grade IV (Table 3). The CDC and the CCI were moderately to strongly correlated with the OPC (r_s = 0.364–0.802 vs 0.364–0.813; $P < 0.001$) (Table 2). Interestingly, costs were generally very similar in patients with no complications and in those with CDC grade I.

OPC in the OSS Groups

Table 4 shows the differences in OPC with CDC grade, and also an upward trend in the different OSS groups ($P < 0.001$).

The CDC and CCI were moderately to strongly correlated in all groups (r_s = 0.444–0.810 vs 0.445–0.820; $P < 0.001$) (Table 2). In addition, the correlation increased with higher grades of surgical complexity. This correlation was higher in emergency than in scheduled surgery in each OSS group.

OPC According to the Number of Complications

The OPC associated with the number of complications varied depending on the CDC ($P < 0.001$) (Supplemental Digital Content 8, http://links.lww.com/SLA/B631). The CDC and CCI were weakly correlated with the OPC in patients with 2 or 3 complications (r_s = 0.282 vs 0.276; $P < 0.01$) and moderately to strongly correlated with the rest (r_s = 0.443–489 vs 0.444–0.550; $P < 0.001$) (Table 2).

OPC According to Prolonged Postoperative Stay

The OPC increased with higher CDC grade ($P < 0.001$) both in the group with prolonged stay and in the group without. In addition, the difference increased with higher CDC grades. The median OPC was much higher in patients with prolonged stay (Table 5). Strong correlations with the CDC and the CCI were demonstrated both in patients with prolonged stay (r_s = 0.802 vs 0.830; $P < 0.001$) and in those without (r_s = 0.515 vs 0.516; $P < 0.001$) (Table 2).

Initial Operating Room Costs

Higher operating room costs are associated with greater subsequent CDC grades ($P < 0.001$) (Supplemental Digital Content 9, http://links.lww.com/SLA/B631). They presented moderate correlations with the CDC and CCI (r_s = 0.448 vs 0.451; $P < 0.001$) (Table 2).

TABLE 2. Correlations of Clavien-Dindo Classification and the Comprehensive Complication Index with the Overall Postoperative Costs (Total and According to Variables) and With Operating Room Costs

		Spearman Correlation Coefficient		
	N	CDC	CCI	*P*
Operating room costs	1808	0.448	0.451	<0.001
Overall postoperative costs in the series	1808	0.658	0.661	<0.001
Surgical group				
Appendectomy	178	0.426	0.427	<0.001
Colectomy	104	0.802	0.813	<0.001
Hernioplasty	92	0.529	0.532	<0.001
Colecystectomy	175	0.364	0.364	<0.001
OSS group				
Minor	773	0.444	0.445	<0.001
Emergency	172	0.537	0.538	<0.001
Scheduled	601	0.349	0.349	<0.001
With admission	209	0.304	0.304	<0.001
Day surgery	392	0.174	0.174	<0.001
Moderate	618	0.555	0.556	<0.001
Emergency	281	0.608	0.609	<0.001
Scheduled	337	0.417	0.417	<0.001
With admission	321	0.417	0.417	<0.001
Day surgery	16	0.421	0.421	<0.001
Major	368	0.699	0.728	<0.001
Emergency	101	0.779	0.794	<0.001
Scheduled with admission	267	0.711	0.714	<0.001
Major+	49	0.810	0.820	<0.001
Emergency	3	1	1	<0.001
Scheduled with admission	46	0.775	0.759	<0.001
Number of complications				
One	240	0.443	0.444	<0.001
Two-Three	84	0.282	0.276	0.008
Four	92	0.457	0.495	<0.001
≥Five	54	0.489	0.550	<0.001
Prolongation of stay				
No	1411	0.515	0.516	<0.001
Yes	397	0.802	0.830	<0.001

Patients who died were excluded from the analysis.

Multivariate Model

Despite a low R^2, the multivariate analysis models (Table 6) showed associations between the CDC, the CCI, age and time of surgery, and the OPC ($P < 0.001$). Specifically, the higher the CDC and CCI and the longer the surgery time, the higher the OPC; in contrast, the OPC was lower in older patients. The classification of the American Society of Anesthesiologists was associated in the CDC model, but not in the CCI model.

Impact on the OPC of a One-unit Increase in the CDC and the CCI

The increase of 1 grade in the CDC raised the OPC on a (constant) basis in appendectomy by €975.65 [95% confidence interval (CI) 787.64–1163.66, $P < 0.001$), in colectomy by €3618.01 (95% CI 2553.55–4682.47, $P < 0.001$), in hernioplasty by €681.90 (95% CI 532.53–831.27, $P < 0.001$), and in cholecystectomy by €1138.17 (95% CI 966.59–1309.74, $P < 0.001$). As for the CCI, a 1-unit increase raised the OPC in appendectomy by €69.49 (95% CI 54.17–84.82, $P < 0.001$), in colectomy by €313.36 (95% CI 231.78–394.94, $P < 0.001$), in hernioplasty by €71.37 (95% CI 966.59–1309.74, $P < 0.001$), and in cholecystectomy by €116.10 (95% CI 102.66–129.54, $P < 0.001$) (Table 7).

With respect to the OSS groups, the increase of 1 grade in the CDC increased the OPC in minor OSS by €1002.52 (95% CI 900.56–1104.49, $P < 0.001$), in moderate OSS by €2283.34 (95% CI 2052.62–2514.06, $P < 0.001$), in major OSS by €3261.96 (95% CI 2503.93–4020.00, $P < 0.001$), and in major + OSS by €5130.44 (95% CI 3169.16–7091.72, $P < 0.001$). With a 1-unit increase in the CCI, the OPC increased in minor OSS by €86.94 (95% CI 78.27–95.62, $P < 0.001$), in moderate OSS by €183.37 (95% CI 166.61–200.12, $P < 0.001$), in major OSS by €259.33 (95% CI 206.49–312.17, $P < 0.001$), and in major + OSS by €377.26 (95% CI 241.76–512.76, $P < 0.001$) (Table 7).

DISCUSSION

The key results responded to the proposed hypotheses. The CDC and the CCI were associated with all the variables under consideration ($P < 0.001$):

1. The OPC of the general series, the homogeneous surgery groups, and the OSS groups were associated with the number of complications, prolonged postoperative stay, and initial operating room costs.
2. In all groups, the OPC presented an upward trend with increasing CDC grade.

In addition, the Spearman correlation coefficient showed a moderate or strong correlation in these variables, with the sole

TABLE 3. Relation Between the Overall Postoperative Costs of Homogenous Groups of Surgery and Clavien-Dindo Classification Versions 1 and 2

Surgical Group	CDC V1	N	Mean	SD	Min	Max	p25	p50	p75	P^*	$P\dagger$
Appendectomy	No complications	153	721.46	460.32	367.33	3034.57	379.33	758.64	758.66	<0.001	<0.001
	CDC grades I–II	24	2419.26	2166.81	379.33	9858.19	758.66	1749.63	3834.79	<0.001	<0.001
	CDC grades III–IV	1	9272.01	—	9272.01	9272.01	9272.01	9272.01	9272.01	<0.001	<0.001
Colectomy	No complications	41	2258.06	492.77	737.98	3498.74	1896.65	2275.98	2655.31	<0.001	<0.001
	CDC grades I–II	41	3460.17	1660.04	1526.20	9711.31	2549.05	3044.09	3812.12	<0.001	<0.001
	CDC grades III–IV	22	14091.68	20708.25	3044.09	104156.98	6480.29	9826.38	13202.06	<0.001	<0.001
Hernioplasty	No complications	67	432.39	193.57	349.56	1517.30	379.33	379.33	404.08	<0.001	<0.001
	CDC grades I–II	23	810.55	592.92	369.00	2453.92	379.87	758.64	808.16	<0.001	<0.001
	CDC grades III–IV	2	3554.12	3953.41	758.64	6349.61	758.64	3554.12	6349.61	<0.001	<0.001
Cholecystectomy	No complications	152	539.09	296.16	362.08	2275.94	379.33	379.33	758.64	<0.001	<0.001
	CDC grades I–II	20	987.05	591.23	362.81	2275.98	731.79	758.66	1327.65	<0.001	<0.001
	CDC grades III–IV	3	6270.90	3066.86	4220.53	9796.61	4220.53	4795.56	9796.61	<0.001	<0.001
	CDC V2	**N**	**Mean**	**SD**	**Min**	**Max**	**p25**	**p50**	**p75**	P^*	$P\dagger$
Appendectomy	Grade 0	153	721.46	460.32	367.33	3034.57	379.33	758.64	758.66	<0.001	<0.001
	Grade I	15	1143.49	616.10	379.33	2334.61	758.64	1106.97	1593.19	<0.001	<0.001
	Grade II	9	4545.55	2167.05	2275.98	9858.19	3815.32	3980.68	4696.00	<0.001	<0.001
	Grade IIIa	—	—	—	—	—	—	—	—	—	—
	Grade IIIb	1	9272.01	—	9272.01	9272.01	9272.01	9272.01	9272.01	<0.001	<0.001
	Grade IV	—	—	—	—	—	—	—	—	—	—
Colectomy	Grade 0	41	2258.06	492.77	737.98	3498.74	1896.65	2275.98	2655.31	<0.001	<0.001
	Grade I	20	2630.18	669.38	1526.20	3805.87	1962.96	2650.77	3153.81	<0.001	<0.001
	Grade II	21	4250.65	1934.13	1896.65	9711.31	2952.00	3812.12	4950.50	<0.001	<0.001
	Grade IIIa	4	4929.83	1597.49	3044.09	6905.45	3809.26	4884.89	6050.40	<0.001	<0.001
	Grade IIIb	16	11382.63	4700.37	5881.28	22259.18	7410.34	10195.44	14040.02	<0.001	<0.001
	Grade IV	2	54087.74	70808.60	4018.50	104156.98	4018.50	54087.74	104156.98	<0.001	<0.001
Hernioplasty	Grade 0	67	432.39	193.57	349.56	1517.30	379.33	379.33	404.08	<0.001	<0.001
	Grade I	19	652.14	438.08	369.00	2275.98	379.33	428.09	758.66	<0.001	<0.001
	Grade II	4	1562.98	716.10	758.66	2453.92	1030.80	1519.68	2095.17	<0.001	<0.001
	Grade IIIa	1	758.64	—	758.64	758.64	758.64	758.64	758.64	<0.001	<0.001
	Grade IIIb	1	6349.61	—	6349.61	6349.61	6349.61	6349.61	6349.61	<0.001	<0.001
	Grade IV	—	—	—	—	—	—	—	—	—	—
Cholecystectomy	Grade 0	152	539.09	296.16	362.08	2275.94	379.33	379.33	758.64	<0.001	<0.001
	Grade I	16	820.53	457.36	362.81	2149.84	585.69	755.55	758.66	<0.001	<0.001
	Grade II	4	1653.12	654.61	758.66	2275.98	1186.72	1788.92	2119.52	<0.001	<0.001
	Grade IIIa	3	6270.90	3066.86	4220.53	9796.61	4220.53	4795.56	9796.61	<0.001	<0.001
	Grade IIIb	—	—	—	—	—	—	—	—	—	—
	Grade IV	—	—	—	—	—	—	—	—	—	—

*Kruskal-Wallis test.
†Cuzick test: Expenditure is expressed in €.
SD indicates standard deviation.

exception of patients presenting 2 or 3 complications in whom the correlation was minor though significant.

In the multivariate models, despite having a low R^2, P values <0.001 indicated a real relationship between the CDC, the CCI, and OPC. This R^2 value was due to the large variability in costs.

The correlations (r_s) were slightly higher in the CCI than in the CDC. The fact that the correlations increased with more complex levels of surgery makes these tools even more attractive in the case of major surgeries.

The study has several limitations, which are listed below:

1. The economic assessment is limited to the perspective of the hospital. In addition, patient care that did not require hospitalization was not considered.
2. The study did not include readmissions at other hospitals. However, it was carried out at the only public referral hospital in the area.
3. This series includes pathologies and procedures of highly varied severity and complexity. To reduce this bias, interventions were grouped according to their OSS classification.[17] However, this does not completely compensate for the heterogeneity of the procedures in each of the groups. To increase reliability, four groups of prevalent and more homogeneous surgeries were used.
4. The more accurate and careful the recording of morbidity by physicians, the higher the morbidity rates, and thus the poorer the outcomes. It is impossible to determine the subjective influence of this phenomenon.
5. The data on economic costs provided for each patient distributed the costs (pharmacy, analytical tests, prosthetics, and maintenance) equally in all patients on each day of their stay.
6. The analysis was carried out at a single center.

In a systematic review of postoperative complication costs, Patel et al found that most studies underestimate these costs for the following reasons: they do not consider readmissions, the results are measured at 30 days, only interventions at experienced services are evaluated, and complication grading systems are only infrequently used.[1]

TABLE 4. Relation Between the Overall Postoperative Costs of Operative Severity Score Groups and Clavien-Dindo Classification Versions 1 and 2

OSS	CDC V1	N	Mean	SD	Min	Max	p25	p50	p75	P*	P†
Minor	No complications	694	436.86	539.89	111.56	5097.88	209.68	209.68	379.33	<0.001	<0.001
	CDC grades I–II	58	1340.01	1193.36	362.81	4257.31	379.87	758.66	1948.71	<0.001	<0.001
	CDC grades III–IV	21	5723.92	6282.63	758.64	29282.95	2269.37	3883.66	6771.79	<0.001	<0.001
Moderate	No complications	484	853.93	703.03	209.68	5689.95	379.33	737.98	1137.96	<0.001	<0.001
	CDC grades I–II	102	2526.73	2106.11	362.81	12613.47	758.66	2056.47	3320.91	<0.001	<0.001
	CDC grades III–IV	32	13049.77	14363.43	3058.16	73758.27	5345.66	9421.48	13216.69	<0.001	<0.001
Major	No complications	143	1888.31	978.84	369.00	6470.16	1137.99	1896.65	2294.27	<0.001	<0.001
	CDC grades I–II	148	3947.65	2895.33	758.64	20319.34	2275.98	3217.15	4812.02	<0.001	<0.001
	CDC grades III–IV	77	19008.61	33748.04	1754.37	283284.88	7303.61	11228.07	18894.03	<0.001	<0.001
Major+	No complications	16	2251.04	979.89	379.33	4678.79	1787.96	2411.76	2655.31	<0.001	<0.001
	CDC grades I–II	20	5324.63	3797.16	1771.69	18504.67	2689.07	4969.57	6073.94	<0.001	<0.001
	CDC grades III–IV	13	17263.67	16228.35	2322.92	54150.36	7934.93	11089.59	20975.68	<0.001	<0.001
	CDC V2	**N**	**Mean**	**SD**	**Min**	**Max**	**p25**	**p50**	**p75**	***P****	***P*†**
Minor	Grade 0	694	436.86	539.89	111.56	5097.88	209.68	209.68	379.33	<0.001	<0.001
	Grade I	43	855.81	791.56	362.81	3793.30	379.33	758.64	837.18	<0.001	<0.001
	Grade II	15	2728.06	1064.89	758.66	4257.31	1867.20	2707.81	3735.14	<0.001	<0.001
	Grade IIIa	4	2934.33	2639.16	758.64	6771.79	1348.09	2103.45	4520.58	<0.001	<0.001
	Grade IIIb	17	6380.29	6755.00	1266.19	29282.95	2581.99	5030.89	6970.81	<0.001	<0.001
	Grade IV	—	—	—	—	—	—	—	—	—	—
Moderate	Grade 0	484	853.93	703.03	209.68	5689.95	379.33	737.98	1137.96	<0.001	<0.001
	Grade I	59	1539.94	1188.41	362.81	5137.37	746.86	1137.96	2209.09	<0.001	<0.001
	Grade II	43	3880.70	2339.16	758.66	12613.47	2294.06	3320.91	4440.37	<0.001	<0.001
	Grade IIIa	13	7098.12	4256.88	3776.94	18820.09	4172.63	5210.17	8621.02	<0.001	<0.001
	Grade IIIb	16	10701.43	4282.69	3058.16	18167.55	7809.56	10783.84	13216.69	<0.001	<0.001
	Grade IV	3	51364.71	21796.26	30219.41	73758.27	30219.41	50116.46	73758.27	<0.001	<0.001
Major	Grade 0	143	1888.31	978.84	369.00	6470.16	1137.99	1896.65	2294.27	<0.001	<0.001
	Grade I	54	2358.70	882.08	758.64	4172.63	1896.65	2332.49	3039.54	<0.001	<0.001
	Grade II	94	4860.45	3240.19	758.66	20319.34	2865.85	3963.91	5442.45	<0.001	<0.001
	Grade IIIa	15	9520.98	6407.19	3044.09	27386.66	5195.35	6905.45	11695.07	<0.001	<0.001
	Grade IIIb	50	14071.18	8604.09	3519.71	40131.70	7577.90	11313.86	17078.29	<0.001	<0.001
	Grade IV	12	51440.78	78140.42	1754.37	283284.88	13077.39	25230.85	46567.07	<0.001	<0.001
Major+	Grade 0	16	2251.04	979.89	379.33	4678.79	1787.96	2411.76	2655.31	<0.001	<0.001
	Grade I	2	2028.54	363.24	1771.69	2285.39	1771.69	2028.54	2285.39	<0.001	<0.001
	Grade II	18	5690.86	3832.33	1881.13	18504.67	4172.63	5012.17	6644.03	<0.001	<0.001
	Grade IIIa	3	7890.89	1080.59	7182.71	9134.66	7182.71	7355.31	9134.66	<0.001	<0.001
	Grade IIIb	5	12242.08	6062.68	7934.93	22725.52	8209.88	11089.59	11250.48	<0.001	<0.001
	Grade IV	5	27908.94	22664.48	2322.92	54150.36	13107.92	20975.68	48987.81	<0.001	<0.001

*Kruskal-Wallis test.
†Cuzick test. Expenditure is expressed in €.
SD indicates standard deviation.

In the light of Patel et al's findings, in the present study, we took care to carry out the following steps:

1. All complications and their methodology were exhaustively recorded.
2. Complications were classified according to the CDC, and the CCI was calculated.
3. Follow-up was performed at 90 days.
4. Readmissions were taken into account.
5. The procedures were grouped into 4 levels of complexity, and the costs of 4 groups of homogeneous procedures were obtained.

In addition, unlike most economic studies of surgical complications that consider total postoperative stay, in our study, preoperative hospital stay and the initial operating room costs were excluded because this may have introduced a major bias.

Several studies have assessed the incremental cost of postoperative complications in specific procedures.[6–10,21–23] Only a few have evaluated the increase in costs with higher CDC grades.[6–10] In the present study, the OPC increased with the severity of the complications as measured by the CCI and the CDC.

This study validates the CCI from an economic perspective. It also links both the CDC and the CCI with the costs in all the surgical procedures carried out at a general surgery service. These associations have not been reported previously: studies carried out to date have focused on specific and habitually complex procedures. To avoid heterogeneity and to be able to apply statistical studies, it was necessary to group all the operations into 4 grades of complexity.[17]

Our literature review identified only 2 articles that related hospital costs and the CCI: the first paper reported that a 1-point increase in the CCI raised hospital costs by US $980 (95% CI 247–1714, $P = 0.010$), although no more details were given.[11]

Staiger et al studied the relationship of the CCI and costs. Those authors found, among other things, a strong correlation between CCI and costs at 3 months postoperatively ($r_{pears} = 0.70$) in the Zurich cohort and a good correlation with the multicenter international cohort ($r_{pears} = 0.60$). The correlation in the surgical group increased with higher morbidity. In contrast to our study, age was positively related to complications and cost. In addition, the authors developed a cost prediction tool whose linear regression model provided a very good prediction of cost ($R^2 = 0.82$). This tool

TABLE 5. Relation of the Clavien-Dindo Classification Versions 1 and 2 With the Overall Postoperative Costs According to Prolongation of Stay

Prolongation of Stay	CDC V1	N	Mean	SD	Min	Max	p25	p50	p75	P*	P†
No	No complications	1173	603.93	672.69	111.56	6470.16	209.68	379.33	758.64	<0.001	<0.001
	CDC grades I–II	217	2325.04	1615.77	362.81	6698.13	758.66	2106.29	3432.22	<0.001	<0.001
	CDC grades III–IV	21	4542.80	2329.99	758.64	8209.88	2917.05	4574.43	6480.29	<0.001	<0.001
Yes	No complications	164	1915.35	812.91	1065.40	5689.95	1475.97	1609.01	2103.34	<0.001	<0.001
	CDC grades I–II	111	4699.63	3662.66	848.18	20319.34	2226.57	3320.91	6645.50	<0.001	<0.001
	CDC grades III–IV	122	17463.01	28312.23	1735.16	283284.88	7182.71	11002.42	18167.55	<0.001	<0.001
	CDC V2	**N**	**Mean**	**SD**	**Min**	**Max**	**p25**	**p50**	**p75**	**P***	**P†**
No	Grade I	124	1410.67	1048.80	362.81	4172.63	725.60	822.67	2275.98	<0.001	<0.001
	Grade II	93	3544.20	1424.58	758.66	6698.13	2655.27	3459.52	4930.32	<0.001	<0.001
	Grade IIIa	7	4406.91	2053.83	758.64	7355.31	3044.09	4654.40	5266.13	<0.001	<0.001
	Grade IIIb	11	5132.23	2575.63	1266.19	8209.88	2917.05	5881.28	7322.33	<0.001	<0.001
	Grade IV	3	2698.60	1177.89	1754.37	4018.50	1754.37	2322.92	4018.50	<0.001	<0.001
Yes	Grade I	34	2475.30	1091.09	848.18	5137.37	1616.32	2217.83	2988.01	<0.001	<0.001
	Grade II	77	5681.80	3963.44	1302.93	20319.34	2664.76	4130.02	7955.86	<0.001	<0.001
	Grade IIIa	28	8559.00	5574.20	1937.53	27386.66	4508.04	7044.08	10509.55	<0.001	<0.001
	Grade IIIb	77	12831.21	8045.91	1735.16	40131.70	7303.61	10944.57	14877.98	<0.001	<0.001
	Grade IV	17	53107.79	64109.95	9670.13	283284.88	20975.68	33697.71	54150.36	<0.001	<0.001

*Kruskal-Wallis test.
†Cuzick test. Expenditure is expressed in €.
SD indicates standard deviation.

was validated in the local and international cohort. The calculator for cost prediction can be consulted at the website: www.assessurgery.com.[12]

In our study, the OPC was lower in older patients. This result is indeed not intuitive. One factor that may have affected it is the high average age of deceased patients compared with survivors (deceased patients were excluded from the analysis). These patients with multiple and serious complications tended to have high costs, but they were not included in the study so as to avoid bias. The same relation was obtained when we repeated the multivariate analysis. In all probability, other factors influenced this result, but we have not been able to identify them.

From the clinical point of view, the CCI has shown itself to be a good index for the evaluation of postoperative morbidity, and also performs better than the CDC in patients with 2 or more complications.[4,5] In our study, the CCI and the CDC were related to the cost parameters considered. This economic evaluation carried out from the hospital perspective supports the use of the CCI in the audit of complications in general surgery services, because it obtains a better association with the clinical results than the CDC and a slightly higher association with the economic results.

In theory, the CCI can be used to compare cost-effectiveness at different services. However, other key parameters should be included in the comparison, such as the complexity of the cases, the surgical technique, and the direct and indirect costs incurred at each service. These costs vary depending on the level of complexity of each hospital and thus affect each hospital service and each patient cost.

As has been suggested, the CCI could be used to compare hospitals with respect to surgical quality and cost-effectiveness in the management of complications.[24] Evaluations of different centers have shown that those that spend more are not necessarily the ones that achieve the best clinical outcomes in patients rescued from perioperative complications.[25] We cannot generalize the results of this study to other settings; however, given our indication of the possible biases, the strict methodology we used to record complications, the calculation of postoperative costs up to 90 days (ie,

TABLE 6. Multivariate Analysis of the Overall Postoperative Costs Adjusted for the Clavien-Dindo Classification and the Comprehensive Complication Index

			95% Confidence Interval	
Overall Postoperative Costs	Coefficient	P	Lower	Upper
CDC	3163.58	0.000	2821.39	3505.77
Age	−21.86	0.048	−43.49	−0.23
ASA	820.36	0.007	226.32	1414.40
Surgical time	13.00	0.000	7.51	18.50
Constant	−889.32	0.115	−1994.70	216.06
R^2	25.53%	—	—	—
CCI	218.42	0.000	198.23	238.61
Age	−22.83	0.018	−41.73	−3.92
Surgical time	19.02	0.000	13.53	24.52
Constant	331.67	0.554	−768.30	1431.64
R^2	30.07%	—	—	—

ASA indicates American Society of Anesthesiologists; R^2, coefficient of determination.

TABLE 7. Impact on Overall Postoperative Costs of the Increase of 1 Grade in the Clavien-Dindo Classification and of 1 Unit in the Comprehensive Complication Index

			95% Confidence Interval	
	Coefficient (€)	*P*	Lower	Upper
Total series (crude model)				
Increase in 1 grade on the CDC	3.037.64	<0.001	2.792.88	3.282.39
Constant	421.32	0.045	8.98	833.67
Increase in 1 point on the CCI	243.81	<0.001	226.08	261.53
Constant	429.01	0.034	332.59	824.76
Surgical group				
Appendectomy				
Increase in 1 grade on the CDC	975.65	<0.001	787.64	1163.66
Constant	761.48	<0.001	610.13	912.83
Increase in 1 point on the CCI	69.49	<0.001	54.17	84.82
Constant	808.78	<0.001	652.00	965.55
Colectomy				
Increase in 1 grade on the CDC	3618.01	<0.001	2553.55	4682.47
Constant	47.12	0.968	−2289.62	2383.86
Increase in 1 point on the CCI	313.36	<0.001	231.78	394.94
Constant	84.71	0.938	−2073.74	2243.16
Hernioplasty				
Increase in 1 grade on the CDC	681.90	<0.001	532.53	831.27
Constant	342.78	<0.001	222.16	463.41
Increase in 1 point on the CCI	71.37	<0.001	56.86	85.89
Constant	342.77	<0.001	227.38	458.15
Colecystectomy				
Increase in 1 grade on the CDC	1138.17	<0.001	966,59	1309,74
Constant	473.92	<0.001	374,29	573,54
Increase in 1 point on the CCI	116.10	<0.001	102.66	129.54
Constant	469.23	<0.001	384.15	554.31
OSS group				
Minor				
Increase in 1 grade on the CDC	1002.52	<0.001	900.56	1104.49
Constant	429.50	<0.001	339.38	519.63
Increase in 1 point on the CCI	86.94	<0.001	78.27	95.62
Constant	448.82	<0.001	359.84	537.80
Moderate				
Increase in 1 grade on the CDC	2283.34	<0.001	2052.62	2514.06
Constant	670.91	0.034	372.72	969.11
Increase in 1 point on the CCI	183.37	<0.001	166.61	200.12
Constant	719.45	<0.001	437.14	1001.77
Major				
Increase in 1 grade on the CDC	3261.96	<0.001	2503.93	4020.00
Constant	676.20	0.522	−1395.86	2748.27
Increase in 1 point on the CCI	259.33	<0.001	206.49	312.17
Constant	533.68	0.591	−1418.02	2485.39
Major+				
Increase in 1 grade on the CDC	5130.44	<0.001	3169.16	7091.72
Constant	−1695.28	0.619	−8484.28	5093.72
Increase in 1 point on the CCI	377.26	<0.001	241.76	512.76
Constant	−1599.84	0.622	−8074.87	4875.18

Expenditure is expressed in €.

excluding preoperative stays and costs), and the estimation of readmission costs, the study will be easy to reproduce at other surgical services. We invite other researchers to carry out external economic validations of the CCI. A comparison of data across hospitals may provide actionable insights.

Like other authors,[1] we consider that to obtain valid assessments of the impact of postoperative complications on costs, complications must be systematically recorded and a detailed breakdown must be carried out of all the costs associated with each patient.

Transparency in health outcomes is an ethical obligation. At a time when attempts are being made to centralize certain complex surgical procedures, the Health Authorities still do not evaluate postoperative morbidity and the costs it produces. As we have seen, the cost of postoperative complications is high. In a society in which health resources are limited, studies of this kind are necessary to identify the services that carry out particular surgical procedures in the most cost-efficient way. We can only talk about benchmarking services if we have access to accurate data, and the use of numerical indexes that quantify complications, such as the CCI, can help us in achieving this objective.

In studies of this kind, we recommend the following measures to reduce bias and in general optimize the research.

With regard to complications:

a. A complication should be considered as any negative event occurring in a patient during hospitalization.[2,13,14]
b. Exhaustive, impartial recording of all complications should be performed.
c. The CDC and CCI should be used for their classification.
d. The analysis should last until 90 days postsurgery, and all readmissions due to complications should be included.
e. Comparisons between centers or services should involve patients who are very similar. This should be established on the basis of a risk adjustment using complexity or severity scores such as the Charlson comorbidity scale.[26] It is also essential to compare surgical procedures of similar complexity and technical difficulty.

With regard to the costs:

a. Preoperative and initial operating room costs should not be included in the assessment of the complications.
b. The cost of the resources consumed by each specific patient should be quantified. It is also essential that the surgical costs of the various surgeries should not just be calculated in terms of surgical time, but should also include the specific costs of the operation including all resources consumed such as prostheses, sutures, and devices.
c. The hospital's level of care should be considered because it may have an influence on the direct and indirect costs incurred at each service.

CONCLUSIONS

In summary, the results of an exhaustive, prospective evaluation of complications and their real cost at different services will help us to propose measures for clinical improvements and to optimize the allocation of financial resources in health services.

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