

## Comparative Analysis of Surgical Approach in Adrenal Surgery

Acín-Gándara Débora<sup>1\*</sup>, Pereira-Pérez Fernando<sup>1</sup>, Medina-García Manuel<sup>1</sup>, Alonso-Gómez S<sup>1</sup>, López-Fernández P<sup>1</sup>, Sebastián-Viana T<sup>2</sup>, García-Muñoz Nájara A<sup>2</sup> and Carrión-Álvarez L<sup>1</sup>

<sup>1</sup>General and Digestive Surgery, Hospital Universitario de Fuenlabrada, Fuenlabrada, Madrid, Spain

<sup>2</sup>Innovation and Development Supervisor, Hospital Universitario de Fuenlabrada, Fuenlabrada, Madrid, Spain

**\*Corresponding Author:** Acín-Gándara Débora, Department of Surgery, Hospital Universitario de Fuenlabrada, Fuenlabrada, Madrid, Spain.

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### Abstract

**Purposes:** Review of our experience, immediate post-operative outcome and indication for laparoscopic approach for adrenal surgery in our surgical department, doing a comparative analysis of surgical approach (laparoscopic, open or converted).

**Methods:** We carried out a descriptive study of forty-eight consecutive patients with adrenal surgery performed between January 2005 and December 2013 and divided into three groups according to the surgical approach (laparoscopic, open or converted). We have analysed the whole sample and the association between the type of surgery (laparoscopy, converted or open) and the other variables (indications, surgical technique, complications and long-term outcome).

**Results:** There were 30 (62.5%) women and 18 (37.5%) men with a median age of 51 (19 - 74) years. Indications for surgery were: 28 functioning adrenal tumours and 20 non-functioning tumours of > 4 cm in size or with suspected malignancy on imaging. Thirty-five (72.9%) procedures were carried out by transperitoneal laparoscopy, 9 (18.8%) were performed through an open route and 4 (8.3%) were converted from laparoscopic to an open approach. Median (IQR) length of stay was 3 (2 - 4) days for laparoscopic procedures and 7 (5 - 11) days for open procedures (p = 0.001). In 6 (12.5%) cases additional elective procedures were performed: splenectomy, renal nodule biopsy, 2 cholecystectomies, left nephrectomy and a partial caval vein resection in a malignant infiltrating pheochromocytoma. Median (IQR) surgical time was 164 (129 - 210) minutes: 137 (120 - 182) minutes for laparoscopic, 201 (185-234) minutes for converted and 215 (181 - 231) minutes for open procedures respectively (p = 0.001). Median (IQR) size of the adrenal surgical specimen was 6 cm (2.5 - 14) and median (IQR) tumor size was 4 cm (2.5 - 4.8). There was an 8.3% morbidity rate (Clavien's grade II and IIIa) and no mortality.

**Conclusions:** In our experience, laparoscopic transperitoneal adrenalectomy has proven to be a safe procedure. Our length of stay and morbidity rate is comparable to those described in the literature. We consider that the laparoscopic approach is currently the technique of choice except in cases of adrenal infiltrating carcinoma or large tumours that require extended resection of surrounding organs. In fact, in our comparative analysis, we have found less surgical time and length of postoperative hospital stay than in the open or converted approach.

**Keywords:** Surgical Approach; Adrenal Surgery

### Introduction

Minimally invasive adrenalectomy is nowadays considered the "gold standard" for the resection of benign and selected malignant adrenal neoplasms. However, until 1992, when Gagner [1] described this technique, adrenal tumours were treated uniformly with open surgery. There is still controversy regarding the optimal surgical approach for adrenal malignant tumors, specially in primary neoplasms, due to the concern with potential capsular disruption and peritoneal dissemination, although the magnitude of this risk is presently

unknown [2,3]. Laparoscopy is currently contraindicated in patients with locally advanced tumours in which resection of surrounding organs may be required. However, some surgeons with extensive experience consider this technique feasible in potentially malignant adrenal tumours when they are well encapsulated, since it can be converted to open surgery if there is an intraoperative suspicion of local infiltration.

### Materials and Methods

Forty-eight consecutive patients who underwent surgery for adrenal disease between January 2005 and December 2013 were registered. The variables analyzed in the study were: gender, age, patient characteristics, surgical indication, surgical technique, surgical approach, conversion to open surgery, right or left adrenalectomy, histopathological diagnosis, imaging tests, tumour size measured by computed tomography (CT), surgical time and postoperative complications. Post-operative and global length of hospital stay was also calculated.

The association between the type of surgery (laparoscopy, converted or open) with the other variables was analysed.

### Statistical analysis of the data

A descriptive study of the group of patients was carried out to establish their socio-demographic characteristics. Qualitative variables were described with their frequency distribution and compared using the Pearson  $\chi^2$  test. Wherever the necessary conditions for this test were not present, the Fisher exact test was used instead. The quantitative variables were analysed using the Student t-test when the figures followed a symmetric data distribution and the Mann-Whitney U test if they didn't. The quantitative variables were described with median and interquartile range, after a non-symmetric distribution of these variables was demonstrated against theoretical models using the Kolmogorov - Smirnov test for normality.

For quantitative variables distributed in more than two groups, the non-parametric Kruskal-Wallis method and median test were applied.

In all cases, the variable distribution has been tested against theoretical models and in statistical hypothesis testing, the null hypothesis has been rejected with a type I error or  $\alpha$  value of less than 0.05.

The program SPSS version 21, was used for statistical interpretation.

### The technical points of adrenalectomy

Laparoscopic adrenalectomy is performed transperitoneally. The patient is placed in lateral decubitus position with the affected side elevated around 60°. The surgeon is located on the abdominal side of the patient. The assistant stands opposite to the surgeon. Pneumoperitoneum is achieved using 11 mm optical trocar under direct vision in the subcostal anterior axillary line. Three additional trocars are inserted: two 5 mm trocars in medioclavicular line and middle axillary line and one 12 mm trocar in posterior axillary line. We use a 30° camera and the CO<sub>2</sub> pressure is regulated between 12 and 15 mmHg throughout the procedure. The first step in left adrenalectomy requires mobilization of pancreas-spleen to the middle line. The dissection of the gland is performed after the adrenal vein has been controlled (specially in pheochromocytoma cases).

The first step in right adrenalectomy is the division of the right triangular ligament of the liver. At this point, the subhepatic inferior vena cava (IVC) should be identified. Once the right adrenal vein is encountered, this vessel is divided between double 5-mm locking polymer clips. Dissection of the gland is subsequently carried out with care taken at the medial aspect where the wall of the IVC stands closely to the adrenal gland. All specimens are extracted in a bag, to avoid the potential spread of tumour cells, through one of the holes of the trocars that is enlarged to allow the removal of the specimen.

Open adrenalectomy is performed through a subcostal incision and it is indicated when any complex associated procedure is required, when there is suspicion of malignancy with likely infiltration of surrounding tissues and in cases with large tumours or those with previous complex abdominal surgery that preclude laparoscopy. The surgical technique for open adrenalectomy is the same as the laparoscopic technique previously described.

## Results

### Descriptive analysis

There were 30 (62.5%) female and 18 (37.5%) male patients that underwent adrenalectomy at our center; the median (IQR) age was 52 years (44 - 61). The lesions were localized on the right side in 21 (43.8%) patients and on the left side in 27 (56.2%) patients.

The surgical indications were: 28 (58%) functioning adrenal tumours, [13 (27%) Cushing syndrome, 8 (17%) pheochromocytomas and 7 (14%) Conn syndrome] and 20 (42%) non-functioning tumours of > 4 cm in size or with suspected malignancy on imaging.

Regarding comorbidities, 38 (79.2%) patients had hypertension, 9 (18.8%) type-2 diabetes, 26 (54.2%) dyslipidaemia, 25 (52.1%) obesity, 32 (66.7%) were active smokers, 11 (22.1%) had a history of heart disease and 12 (34.3%) had had a previous abdominal surgery.

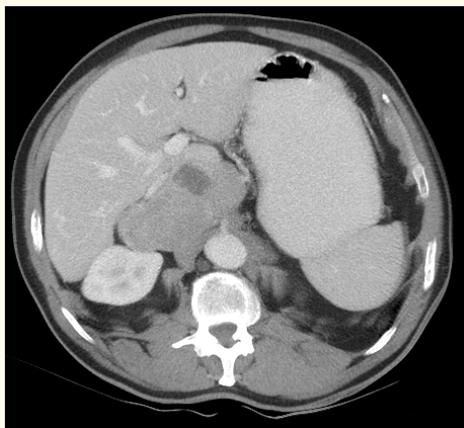
Eleven (22.9%) patients were asymptomatic and 37 (77.1%) symptomatic, highlighting 19 (39.6%) patients that were studied for new onset hypertension, 9 (18.8%) for suspected symptoms of Cushing syndrome, 6 (12.5%) for abdominal pain and 3 (6.3%) others. In all patients laboratory test were performed to rule out a pheochromocytoma, including a 24-hr urine fractionated metanephrines and catecholamines test and fractionated plasma free metanephrines test. Likewise, a plasma aldosterone concentration and renin activity test as well as a 24-hr urinary free cortisol test was performed, using 1 mg overnight dexamethasone suppression in patients with symptoms of Cushing's syndrome.

All patients were studied with the following imaging examinations: 47 (98%) with abdominal CT, ultrasound in 14 (29%), 19 (39%) with magnetic resonance imaging (MRI), 12 (25%) with MIBG scintigraphy, 1 (2%) with PET-CT and 1 (2%) with arteriography.

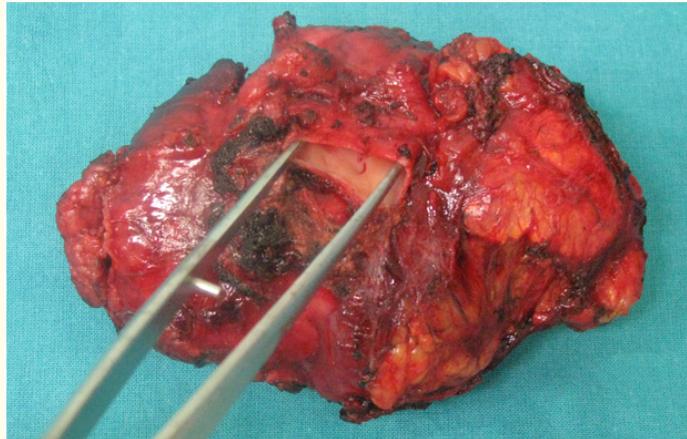
### Comparative analysis

We have compared three groups according to the surgical approach (laparoscopic, open or converted). Thirty-four patients (72.9%) underwent laparoscopic adrenalectomies, in 9 patients (18.8%) an open adrenalectomy was carried out and 4 (8.3%) were converted cases.

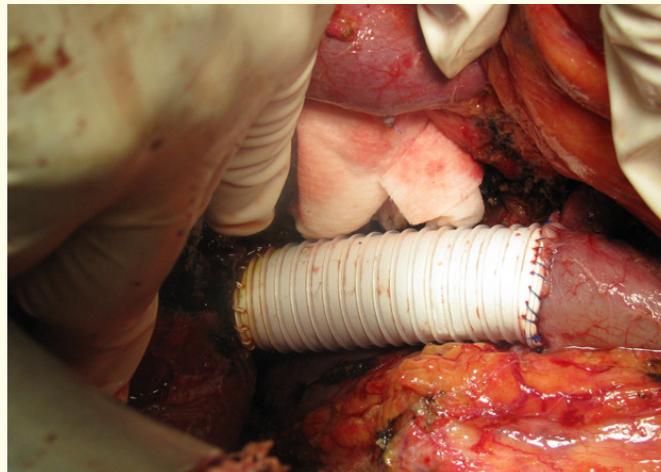
Laparotomy was indicated in four cases for suspected malignancy, in two cases due to tumour size of > 9 cm and in three cases due to the need to perform a combined complex surgical procedure (one caval vein replacement after combined caval and caudate lobe resection; one large left tumour in which a nephrectomy was needed; and a large tumor that required a combined splenectomy). An additional procedure was performed in six cases (12.5%), one laparoscopic and five open: one splenectomy, one biopsy of a renal nodule, two cholecystectomies, one left nephrectomy and one circumferential partial resection of caval vein due to an invasive malignant pheochromocytoma and its replacement with a vascular prosthesis (Figure 1-4).



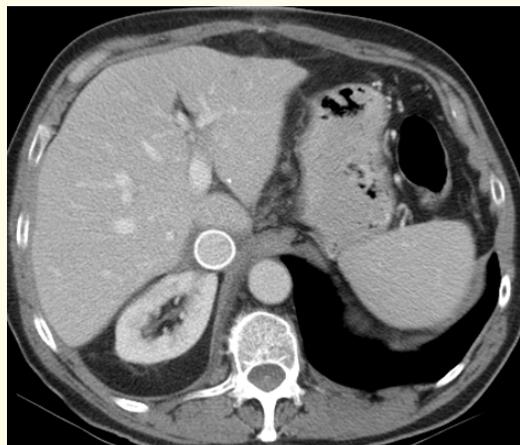
**Figure 1:** Abdominal CT: an invasive malignant pheochromocytoma.



**Figure 2:** Right adrenalectomy with circumferencial partial resection caval vein because of an invasive malignant pheochromocytoma.



**Figure 3:** Its replacement with a vascular prosthesis.



**Figure 4:** Abdominal CT: vascular prosthesis.

Table 1 shows the characteristics of each group of patients according to the type of surgical approach.

Converted n = 4		Surgical Approach			Total n = 48	p
		Open n = 9	Laparoscopic n = 35			
Age (years) Median (IQR)		54 (36 - 62)	45 (29 - 52)	52 (47 - 64)	52 (44 - 61)	0.09
Tumor size (cm) Median (IQR)		7.3 (3.1 - 10.8)	4.8 (3.7 - 9.3)	3.1 (2.4 - 4.2)	4 (2.5 - 4.8)	0.01
Gender n (%)	Men	1 (25)	4 (44.4)	13 (37.1)	18 (37.5)	0.89
	Women	3 (75)	5 (55.6)	22 (62.9)	30 (62.5)	
Hypertension n (%)	No	0 (0)	4 (44.4)	6 (17.1)	10 (20.8)	0.17
	Yes	4 (100)	5 (55.6)	29 (82.9)	38 (79.2)	
Dyslipidemia n (%)	No	3 (75)	6 (66.7)	13 (37.1)	22 (45,8)	0.14
	Yes	1 (25)	3 (33.3)	22 (62.9)	26 (54.2)	
Type - 2 - diabetes n (%)	No	3 (75)	8 (88.9)	28 (80)	39 (81,3)	1
	Yes	1 (25)	1 (11.1)	7 (20)	9 (18.7)	
Obesity n (%)	No	1 (25)	6 (66.7)	16 (45.7)	23 (47,9)	0.35
	Yes	3 (75)	3 (33.3)	19 (54.3)	25 (52.1)	
Heart disease n (%)	No	3 (75)	9 (100)	25 (71.4)	37 (77,1)	0.13
	Yes	1 (25)	0 (0)	10 (28.6)	11 (22.9)	
Smoker n (%)	No	1 (25)	5 (55.6)	10 (28.6)	16 (33,3)	0.35
	Yes	3 (75)	4 (44.4)	25 (71.4)	32 (66.7)	
Previous abdominal surgery n (%)	No	2 (50)	4 (44.4)	23 (65.7)	29 (60,4)	0.48
	Yes	2 (50)	5 (55.6)	12 (34.3)	19 (39.6)	
Adrenalectomy n (%)	Right	3 (75)	4 (44.4)	14 (40)	21 (43,8)	0.48
	Left	1 (25)	5 (55.6)	21 (60)	27 (56.2)	

**Table 1:** Descriptive study of the group of patients to establish their socio - demographic characteristics according to the type of surgical approach: age, gender, hypertension, dyslipidemia, Type - 2 - diabetes, obesity, heart disease, smoker, previous abdominal surgery, right or left adrenalectomy. The qualitative variables are described with their frequency distribution and the quantitative variables are described with median and interquartile range.

The median (IQR) global operative time was 163.5 minutes (129.3 - 209.5), with a minimum time of 65 minutes and a maximum time of 420 minutes.

The median (IQR) operative time in laparoscopic adrenalectomies was 137 minutes (120 - 182) and the conversion rate was 8.3% (four patients), due to technical difficulty (in two cases) and large tumour size (two cases, being one of them an adrenal carcinoma with invasion of adjacent structures detected intraoperatively). In converted cases median (IQR) operative time was 201 min (185 - 234) and in open cases was 215 minutes (181 - 231) p = 0.001 (Table 2).

	Surgical Approach			Total	p
	Converted n = 4	OPEN n = 9	Laparoscopic n = 35		
Follow up (months) Median (IQR)	16.7 (4.4 - 44.8)	27.7 (9.9 - 65.1)	24.5 (9.6 - 64.2)	25.02 (9.2-60.4)	0.7
Surgical time (minutes) Median (IQR)	201 (185 - 234)	215 (181 - 231)	137 (120 - 182)	163.5 (129.3 - 209.5)	0.001
Postoperative stay (days) Median (IQR)	3.5 (3 - 7.8)	7 (5 - 11)	3 (2 - 4)	4 (2.6 - 5.8)	0.001
Global stay (days) Median (IQR)	3.5 (3 - 8.5)	7 (6.5 - 14)	3 (2 - 5)	4 (3 - 7)	0.003
Complications n (%)	0 (0)	1 (2.1)	3 (6.2)	4 (8.3)	1

**Table 2:** Follow up, surgical time, postoperative, stay, global stay and complications. The qualitative variables are described with their frequency distribution and the quantitative variables are described with median and interquartile range.

The pathological findings were: 29 adrenal cortical adenomas, 8 pheochromocytomas (one malignant), 3 cortical hyperplasia, 2 epithelial cysts, 2 carcinomas, 1 neoplasm with uncertain malignant potential, 1 ganglioneuroma, 1 myofibroblastic tumor, 1 myelolipoma and 1 schwannoma.

The median (IQR) adrenal size was 6 cm (2.5 - 14) and the median (IQR) tumor size was 4 cm (2.5 - 4.8), with a minimum size of 1.2cm and a maximum size of 12.6 cm.

Four patients had the following complications (morbidity rate 8.3 percent): pulmonary thromboembolism (Clavien-Dindo II), pneumonia (Clavien-Dindo II), intra-abdominal collection requiring percutaneous drainage (Clavien-Dindo IIIa), and gastrointestinal haemorrhage secondary to portal hypertension in a patient with previous Budd-Chiari’s syndrome requiring placement of TIPS (Clavien-Dindo IIIa). There were no statistically significant differences in complications between groups (p > 0,05). There was no postoperative mortality.

The median (IQR) length of postoperative hospital stay was 4 days (2.3 - 5.8): 3 (2 - 4) days in laparoscopic procedures, 3.5 (3 - 7.8) days in conversion procedures and 7 (5 - 11) days in open procedures (p = 0.001) (Table 2).

**Discussion**

Laparoscopic surgery is currently considered the “gold standard” for the resection of functioning benign tumors (causative of hyperaldosteronism or Cushing Syndrome), showing a shorter length of hospital stay, lower complication rate and increased patient satisfaction, with the same efficacy and safety as open surgery [4,5]. In our series, although it is a small sample and overall lower postoperative stay in the laparoscopic surgery group was observed. However, no statistically significant difference in the postoperative complication rate was found.

Laparoscopic approach for malignant adrenal pathology, however, is still considered controversial. Although traditionally most authors choose open surgery for adrenal carcinoma, which allows “en block” resection with less risk of tumour cells spread, some recent publications propose the laparoscopic approach in malignant tumours without apparent infiltration of adjacent organs, showing similar results in terms of local recurrence and distant metastases in the hands of skilled surgeons [3,6,7].

Evidently, a very careful dissection is essential to avoid the rupture of the capsule, therefore avoiding tumour cells spread. For the same reason, a bag for the removal of the surgical specimen must be used. When the adrenal tumor is a metastasis from another origin, there is much less controversy and laparoscopic approach is accepted in this scenario [8].

In our series, we have operated on two patients with malignant disease, both with open surgery. One adrenal carcinoma with a large tumor that infiltrates adjacent organs and another by initial laparoscopic approach but later converted to open surgery because of the infiltration of adjacent structures, and the other a malignant pheochromocytoma of 9.5 cm, with capsular infiltration and extension to adipose tissue, which required vena cava resection and its replacement with a vascular prosthesis.

Regarding the long-term outcome of the two patients with adrenal carcinoma, one of them presented local recurrence and distant metastases (liver) 5 months after surgery, and died 12 months after the operation. The other one is alive and disease-free 84 months after the operation. The patient with malignant pheochromocytoma, had a local recurrence, which was resected 29 months after the first surgery (currently alive and disease-free, 78 months after the operation).

In the literature, a mortality below 1% and morbidity of 8-19% has been described in different series [9-12]. Conversion rate in our center was slightly higher than that published in the Spanish national survey in 2011 [12] (6.7% vs 8.3% in our hospital), but nevertheless similar or lower than that reported by other authors [13,14]. Median (IQR) surgical time in our cohort was 163.5 minutes (129.2 - 209.5), which seems high compared to other series, but we must emphasize the associated complex procedures in several cases that increased surgical time. As one might expect, the surgical time of the laparoscopic approach was lower than that of the open or converted approaches.

If we focus just on the cases performed by laparoscopy, median (IQR) surgical time was 137 minutes (120 - 182), similar to other series such as Lamas, *et al.* (131 minutes with a range 60 - 240) [14] which also shows similar adrenal size (6 cm). The morbidity was similar (8.3% in our series vs 8.9% in Lamas') as was the mortality rate (0% vs 0.3%). Median hospital stay (4 days vs 4.9 days) and reoperation rate (0% vs 2.3%) were slightly better in our series.

The percentage of laparoscopic adrenalectomies is similar to other published series.

### Conclusions

We consider laparoscopic surgery to be the best approach for adrenalectomy, except in cases of adrenal carcinoma or large size tumors requiring resection of adjacent organs. Based on our experience, this technique can be considered safe, with a length of hospital stay and complication rate similar to those published in the literature. In fact, in our comparative analysis, we have found less surgical time and length of postoperative hospital stay than in the open or converted approach.

Open adrenalectomy is reserved for large tumors, for suspected adrenal carcinoma with invasion of adjacent organs or when complex associated procedures are required, as in the one reported in our series in which vena cava replacement was needed.

### Conflict of Interest Statement

Débora Acín Gándara M.D, PhD. and other co-authors have no conflict of interest.

### Bibliography

1. Gagner M., *et al.* "Laparoscopic Adrenalectomy in Cushing's syndrome and pheochromocytoma". *New England Journal of Medicine* 327.14 (1992): 1033.
2. Rodríguez JL, *et al.* "Evolution of laparoscopic adrenal surgery in a general surgery department". *Cirugía Española* 83.4 (2008): 205-210.

3. Smitn CD., *et al.* "Laparoscopic adrenalectomy: new gold standard". *World Journal of Surgery* 23.4 (1999): 389-396.
4. Aguilera A., *et al.* "Laparoscopic adrenalectomy. Five-year experience". *Actas Urológicas Españolas* 34.2 (2010): 181-185.
5. Henry HF., *et al.* "Results of laparoscopic Adrenalectomy for Large and Potentially Malignant Tumors". *World Journal of Surgery* 26.8 (2002): 1043-1047.
6. Harrison BJ. "Surgery of adrenocortical cancer". *Annales d'Endocrinologie* 70.3 (2009): 195-196.
7. Gonzalez RJ., *et al.* "Laparoscopic resection of adrenal cortical carcinoma: a cautionary note". *Surgery* 138.6 (2005): 1078-1085.
8. Strong VE., *et al.* "Laparoscopic adrenalectomy for isolated adrenal metastasis". *Annals of Surgical Oncology* 14.12 (2007): 3392-3400.
9. Young Jr WF. "Clinical practice. The incidentally discovered adrenal mass". *New England Journal of Medicine* 356.6 (2007): 601-610.
10. Brunaud L., *et al.* "Observation or laparoscopic adrenalectomy for adrenal incidentaloma? A surgical decision analysis". *Medical Science Monitor* 12.9 (2006): 355-362.
11. Gonzalez R., *et al.* "Laparoscopic approach reduces likelihood of Perioperative complications in patients undergoing adrenalectomy". *American Surgeon* 70.8 (2004): 668-674.
12. Villar JM., *et al.* "Adrenal surgery in Spain: final results of a national survey". *Cirugía Española* 89.10 (2011): 663-669.
13. Maestre-Maderuelo M., *et al.* "Laparoscopic adrenalectomy: the best surgical option". *Cirugía y Cirujanos* 81.3 (2013): 196-201.
14. Lamas S., *et al.* "Laparoscopic adrenalectomy: causes of conversion, personal experience and literature review". *Cirugía Española* 75.1 (2004): 18-22.

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