

Laparoscopic adrenalectomy for functioning and non-functioning adrenal tumours

Adrenalektomia laparoskopowa u pacjentów z hormonalnie czynnymi i nieczynnymi guzami nadnerczy

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Abstract

Background: The purpose of this study was a retrospective analysis of outcomes following laparoscopic adrenalectomy (LA) performed for benign adrenal tumours responsible for various endocrinological disorders. The patients were diagnosed with non-functioning (NFT) and functioning adrenal tumours (FT) including pheochromocytoma (PH), Conn's syndrome (CO) and Cushing's (CS) syndrome.

Material and methods: A total of 165 LAs were carried out between August 1995 and September 2009 via either the transperitoneal (n = 38) or retroperitoneal (n = 127) approach. The analysed factors included demographic data of patients, the American Association of Anaesthesiology score (ASA), indication for surgery, tumour size and side, intraoperative and postoperative outcome of LA including duration of surgery, blood loss, time until ambulation, length of hospital stay, time until return to normal activity, the complication rate, as well as the conversion rate to open adrenalectomy.

Results: There were 111 patients with NFT and 54 with FT. Patients with NFT were significantly older than those with CO (p < 0.05). The mean size of the lesion differed between CO and other adrenal tumours (p < 0.05) as well as between NFT and PH (p < 0.05). All the lesions except aldosteronomas were detected predominantly in the right adrenal gland (p < 0.05). However, despite the different characteristic and clinical disorders related to laparoscopically removed adrenal tumours, the intraoperative and postoperative outcomes did not significantly differ in most cases between the analysed groups of patients.

Conclusion: This study shows that LA is a safe, effective, and well-tolerated procedure despite the hormonal activity of the removed lesions. Minimal invasive surgery may be recommended as the 'gold standard' in the treatment of both functioning and non-functioning benign tumours of the adrenal gland. (**Pol J Endocrinol 2011; 62 (6): 512–516**)

Key words: laparoscopic adrenalectomy, functioning adrenal tumours, non-functioning adrenal tumours

Streszczenie

Wstęp: Celem tego badania była retrospektywna analiza wyników adrenalektomii laparoskopowej (LA) wykonywanej z powodu łagodnych guzów nadnerczy mogących powodować różne zaburzenia endokrynologiczne. U pacjentów rozpoznawano nieczynne hormonalnie guzy nadnerczy (NFT) oraz hormonalnie czynne guzy nadnerczy (FT), w tym guz chromochłonny (PH), zespół Conna (CO) i zespół Cushinga (CS).

Material i metody: Pomiędzy sierpniem 1995 r. a wrześniem 2009 r. wykonano łącznie 165 LA z dostępu przezotrzewnowego (n = 38) lub zaotrzewnowego (n = 127). Analizowanymi czynnikami były: dane demograficzne pacjentów, wynik skali ASA, wskazanie do operacji, rozmiar guza i jego umiejscowienie, śródoperacyjne i pooperacyjne wyniki LA w tym czas trwania operacji, utratę krwi, czas uruchomienia chorych, długość hospitalizacji, czas powrotu do normalnej aktywności, śródoperacyjne i pooperacyjne powikłania, jak również wskaźnik konwersji do otwartej adrenalektomii.

Wyniki: Badaniem objęto 111 pacjentów z NFT i 54 z FT. Pacjenci z NFT byli istotnie starsi niż pacjenci z CO (p < 0,05). Średnia wielkość zmiany różniła się pomiędzy CO i innymi guzami nadnerczy (p < 0,05), jak również pomiędzy NFT i PH (p < 0,05). Wszystkie zmiany za wyjątkiem *aldosteronoma* wykrywano głównie w prawym nadnerczu (p < 0,05). Mimo różnych cech charakterystycznych oraz zaburzeń klinicznych związanych z usuwanymi laparoskopowo guzami nadnerczy w większości przypadków nie było istotnych różnic wyników środoperacyjnych i pooperacyjnych pomiędzy analizowanymi grupami pacjentów.

Wnioski: Przedstawione badanie pokazuje, że LA jest bezpiecznym, efektywnym i dobrze tolerowanym przez chorych zabiegiem mimo czynności hormonalnej usuwanych zmian ogniskowych. Małoinwazyjny zabieg operacyjny można uznać za metodę referencyjną w chirurgii zarówno czynnych, jak i nieczynnych hormonalnie łagodnych guzów nadnerczy. (Endokrynol Pol 2011; 62 (6): 512–516)

Słowa kluczowe: adrenalektomia laparoskopowa, hormonalnie czynne guzy nadnerczy, hormonalnie nieczynne guzy nadnerczy

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Introduction

The first laparoscopic adrenalectomies described in the literature were carried out in 1992 [1, 2]. This minimally invasive procedure is now considered the "gold standard" for the removal of benign functioning and non-functioning adrenal tumours [3–6]. However, it has not been demonstrated unequivocally in the literature whether the hormonal activity of the operated adrenal tumours has any influence on the outcome of LA [7–10].

There are two main laparoscopic approaches used for adrenalectomy. Transperitoneal laparoscopic adrenalectomy (TLA) appears to be the procedure of choice for pheochromocytoma, bilateral adrenal tumours as well as lesions that are larger than 6 cm in diameter [6, 9, 11, 12]. Retroperitoneal laparoscopic adrenalectomy (RLA) is advocated primarily for small functioning and non-functioning adrenal adenomas [13–16].

NFT is considered an indication for surgery if its diameter exceeds 4 cm, while FT is removed regardless of the tumour size [4, 17]. The technical restrictions, however, limit the indications for LA for tumours that are bigger than 12 cm in diameter. Moreover, malignant adrenal tumours, both primary and metastatic, are still considered a controversial indication for minimal invasive surgery [3, 4].

This study was designed primarily to analyse the perioperative results of endoscopic removal of different adrenal tumours in respect of their hormonal secretion. We also aimed to find out if there is an influence of other factors, such as size and side of adrenal tumour, and the patient's age, on the outcome of LA.

Material and methods

A retrospective analysis of the computer database for LAs performed at the Department of General and Transplant Surgery, M. Curie Hospital in Szczecin, Poland was done. Between August 1995 and September 2009, there were 165 LAs performed via either transperitoneal (n = 38) or retroperitoneal (n = 127) approaches. The analysed group included 122 women and 43 men, mean age of 52 (range: 18–79) years. All patients had

Table I. Demographic and tumour characteristicsTabela I. Dane demograficzne i cechy guzów

Side — R/L n (%) **Tumour type** n (%) Mean age (years \pm SD) Mean size (cm \pm SD) NFT 111 (67.3) 56.7 ± 11.5 3.8 ± 1.2 73/38 (66/34) CO 6/19 (24/76) 25 (15.1) 49.9 ± 8.8 2.5 ± 0.8 CS 19 (11.5) 52.1 ±13.0 3.8 ± 1.3 11/8 (58/42) PH 8/2 (80/20) 10 (6.1) 53.3 ± 12.1 $4.6\,\pm\,0.9$

preoperative endocrine evaluation. Their health status was classified according to the American Association of Anaesthesiology score. The indications for surgery were both benign and non-functioning (size > 4 cm or smaller if co-existing with severe blood hypertension) as well as functioning adrenal tumours. Benign bilateral as well as metastatic and primary malignant adrenal lesions removed using LA were excluded from the analysis. The indication for surgery, the patient's age, the tumour side and size, duration of surgery, blood loss, perioperative morbidity, conversion rate to OA, time until ambulation, length of hospital stay and time until return to normal activity were all evaluated. The hospital stay was calculated from the day of surgery. Patients were questioned regarding their return to normal activity during the check-up visit in the outpatient department or via a telephone questionnaire. Return to normal activity included resumption of full-time working, as well as home, social or sport activities.

Transperitoneal laparoscopic adrenalectomy was performed according to the method described by Gagner [2] while extraperitoneal laparoscopic adrenalectomy followed the approach of Whittle [18] and Kelly [19].

The data was analysed employing Kruskal-Wallis test, Mann-Whitney test, χ^2 and Fisher exact test from the computer programs (Statistica 7.1). Differences were considered statistically significant when p < 0.05.

Results

The most frequent indication for LA (Table I) was NFT (67%). The actual physical status of the patients (ASA score) undergoing LA was not significantly (NS) related to the type of endocrinological disorders accompanying the removed adrenal tumour.

The significant difference regarding the mean age of patients with adrenal tumours was observed only between those with NFT and CO (p = 0.008) (Table I). The female to male ratio was similar in all analysed groups of patients (NS).

The mean size of the adrenal lesion (Table I) differed significantly between patients who were treated Table II. Intraoperative outcome of LA. Mean valuesTabela II. Śródoperacyjne wyniki LA. Wartości średnie

Tumour type	Duration of LA (min ± SD)	Blood loss (ml ± SD)
NFT ($n = 111$)	137.8 ± 50.4	152.1 ± 185.3
CO (n = 25)	133.4 ± 42.2	145.6 ± 154.4
CS (n = 19)	144.4 ± 57.1	173.1 ± 238.1
PH (n = 10)	164.5 ± 62.2	149.0 ± 109.6

Table III. Postoperative outcome of LA. Values presented asmeans

Tabela III. Pooperacyjne wyniki LA. Wartości średnie

Tumour type	Time until ambulation (hours ± SD)	Hospital stay (days ± SD)	Return to normal activity (days ± SD)
NFT (n =111)	19.3 ± 9.5	5.2 ± 3.5	15.3 ± 9.6
CO (n = 25)	17.6 ± 8.7	4.6 ± 2.4	13.5 ± 6.7
CS (n = 19)	16.2 ± 9.5	4.4 ± 1.5	17.8 ± 12.8
PH (n = 10)	20.8 ± 5.2	6.9 ± 3.6	18.0 ± 7.0

for CO and other tumours including PH (p = 0.00002), CS (p = 0.001) and NFT (p = 0.00001), and it was also different for NFT *vs.* PH (p = 0.009).

The majority of adrenal tumours were diagnosed in the right adrenal gland, with the exception of CO (p = 0.001).

The mean operative time and blood loss did not significantly depend on the type of removed adrenal lesion (Table II).

There was a significant difference concerning time until ambulation after the operations performed for CS vs. NFT (p = 0.04) and vs. PH (p = 0.02) (Table III). However, the length of hospital stay, as well as the mean time until return to normal activity, were all similar between the analysed groups of patients (NS). The incidence of conversions to OA, as well as the intraoperative and postoperative complication rate, did not differ significantly between the groups (Table IV).

Discussion

Over the last two decades, LA has become the surgical procedure of choice in the treatment of most benign adrenal lesions. This approach is suitable for removal of both FT and NFT [9]. The outcome of these procedures does not appear to depend generally on the manner of hormonal secretion by the adrenal lesion. The tumours responsible for CS and CO, PH and incidentaloma can be successfully operated on laparoscopically despite Table IV. Rate of conversion to OA. The intraoperativecomplication (IC) rate and the postoperative complication(PC) rate

Tabela IV. Wskaźnik konwersji do OA. Wskaźniki powikła	ań
śródoperacyjnych (IC) i pooperacyjnych (PC)	

Tumour type	Conversion rate	IC rate	PC rate
NFT (n = 111)	20 (18.02%)	18 (16.3%)	12 (10.8%)
CO (n = 25)	3 (12.0%)	5 (20.0%)	4 (16.6%)
CS (n = 19)	3 (15.79%)	6 (31.5%)	2 (11.1%)
PH (n = 10)	0 (0%)	2 (20.0%)	2 (20.0%)

their different adrenal origins and varying clinical symptoms [3–5, 10]. Benign NFT, however, should be removed only when its size exceeds 4 cm in diameter [17]. If the NFT is smaller, it is considered an indication for surgery in patients with co-existing and severe blood hypertension [20]. The large size of an adrenal tumour (> 8 cm) and/or the evidence of its local invasiveness (both primary and metastatic adrenal malignancy) are still considered in many centres to be contraindications to a laparoscopic approach [3, 4, 10, 12, 21–23].

The differences in adrenal surgery and its outcome might depend not only on the tumour secretion but also its size and side as well as the age of the patient. These individual features of the adrenal tumour could potentially influence the outcome of the laparoscopic procedure [6, 10]. Moreover, different adrenal lesions can be removed employing any endoscopic approach. Ideally however, the surgical access is matched to the type of adrenal tumour. We believe that in the case of adenomas, the small adrenal lesions can be operated on using lateral or posterior extraperitoneal procedure despite their hormonal activity, while larger ones should be removed by the transperitoneal approach. In the case of surgery for chromaffin tumours, the transperitoneal access is usually required because of the need for an early closure of the adrenal vein. It allows the early occlusion of the vein, avoiding the life-threatening output of catecholamines [6, 9].

NFT occurs more frequently in elderly patients. It is usually discovered incidentally with ultrasound, CT or MR examinations performed for other indications [4]. The functioning adenomas and pheochromocytomas are detected usually because of specific symptoms accompanying the growth of the tumour. They are found more frequently one or two decades earlier than incidentalomas, as was also shown in this study.

Because of the limitations of minimal invasive surgery, the size of the adrenal tumour could have an influence on the performance of the procedure [6]. Many authors have shown that the mean size of the lesion was largest in patients with PH [4, 6, 10]. The mean size of PH was also largest in our series, with the smallest diameter belonging to aldosteronomas. The technique of the procedure for right and left adrenal tumours differs because of the varying anatomy on both sides of the body, but it should not have any important influence on the outcome of surgery [6]. In our analysis, most of the tumours were located on the right side, while aldosteronomas were detected mostly on the left side. Despite the significant difference between the tumour size in a case of CO and other lesions, as well as the predominant left location of CO, we did not observe a significant influence of these factors on the outcome of LA.

In our study, the type of the hormonal secretion of the removed adrenal tumour, its size and side did not have any significant influence on the mean duration of LA or the average blood loss. The review by Gumbs and Gagner of 19 papers with the largest published series of more than 100 LAs, found no influence of hormonal disorder on the operative time, while blood loss was higher for PH [10]. A diagnosis of pheochromocytoma has also been shown by other authors to be associated with increased blood loss. However, duration of surgery, when compared to LA for other indications, was also longer. This may be due to prominent vascularity, larger size and catecholamine output seen in these tumours [6, 24, 25]. Karcher et al. reported that chromaffin tumours larger than 6 cm in diameter are associated with a longer operative time compared to other lesions. Blood loss, rate of intraoperative haemodynamic instability and hospital stay, however, was not associated with the size of these tumours [9].

Our analysis showed that diagnosis of non-functioning adrenal lesions and pheochromocytomas could have a significant influence on the length of time to ambulation of patients undergoing LA. Similar findings have also been reported by other authors [9, 10, 26–28]. Gotoh et al. reported a longer return to normal activity in patients undergoing LA for PH compared to other entities [24]. This was not confirmed in our series.

In our study, we did not observe a significant influence of the type of tumour on the rate of intraoperative and postoperative complications. The commonest complication in our series, as in reports by others, was tissue bleeding [29]. In most cases this could be controlled surgically during LA, but in three cases conversion to open surgery was necessary because the ongoing tissue bleeding did not allow for safe tumour dissection. Lesion of the peritoneum occurred in five patients undergoing extraperitoneal LA. Diaphragmatic injury was observed in three patients and resulted in pneumothorax treated by thoracic drainage. In all cases it occurred during the right extraperitoneal procedure. We had also experienced two severe bleedings from the adrenal or inferior caval vein during removal of the right adrenal lesion. Some authors have observed a higher rate of intraoperative complications for patients operated on for PH [3, 10]. According to others, however, the number of complications related to endoscopic removal of PH depends first of all on the surgeon's experience with advanced laparoscopic procedures, and is comparable to the outcome of LA performed for other hormonal disorders [9, 30].

In most cases, we had minor postoperative complications only. Neuralgia with temporary paresis of the right upper limb and acute adrenal insufficiency were the only severe postoperative disorders. The acute adrenal insufficiency that occurred after the removal of PH resulted in the death of one patient on the fourth postoperative day. This severe complication occurs in slightly more than 1% of patients and is specific for pheochromocytoma [29]. Other authors have also reported a similar complication rate regardless of the type of hormonal disorder associated with the adrenal tumour [4, 6, 10].

Conversion to OA ranges between 0 and 13% [10]. According to many authors, uncontrollable bleeding is the main indication for it [5, 31–33]. In our series, the cause and the rate of conversion to OA did not depend on the underlying hormonal disorder. The most frequent indications to convert the procedure were difficult dissection or detection of the adrenal tumour, ongoing tissue bleeding, lesion of the peritoneum during the extraperitoneal approach, pneumothorax as well as injury of the adrenal or inferior caval vein. The recent meta-analysis by Gumbs and Gagner indicated no significant difference regarding the conversion rate between all types of LA despite the hormonal activity of the removed tumours [10].

Similarly to the complication rate, the number of conversions may mostly depend on the experience of the surgeon rather than the type of hormonal disorder [8, 9, 15, 33, 34]. Shen et al, however, based on an analysis of 456 LAs, found that the size of the tumour, Body Mass Index and the diagnosis of PH are all predictive factors for conversion to OA [35].

In conclusion, this study shows that LA allows for a safe approach to benign adrenal lesions regardless of their different hormonal activity. The outcome of the procedure does not generally depend on the type of hormonal disorder diagnosed with the adrenal tumour. Moreover, pheochromocytoma can be removed laparoscopically with the same safety and efficacy as other benign adrenal lesions.

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