



Original research

Recurrence and functional outcomes of partial adrenalectomy: A systematic review and meta-analysis



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HIGHLIGHTS

- Parathyroidectomy for PHPT potentially improves function and quality of life.
- Currently, there is no quantitative evidence to support this for all studies.
- This study provides evidence that parathyroidectomy improves the quality of life.

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ABSTRACT

Background: Partial adrenalectomy is typically performed for the treatment of hereditary and sporadic bilateral tumours, to reduce the risk of adrenal failure, particularly in younger patients. Partial adrenalectomy proposes a postoperative steroid-free course nevertheless, is associated with the risk of local recurrence. In this study we evaluate the recurrence and functional outcomes of partial adrenalectomy. **Methods:** A systematic search was conducted using MEDLINE, PubMed, EMBASE, Current Contents Connect, Cochrane library, Google Scholar, Science Direct, and Web of Science. The search identified 60 relevant articles reporting on patients who underwent partial adrenalectomy. Data was extracted from each study and used to calculate a pooled event rate and 95% confidence interval (95% CI).

Results: The overall recurrence rate was 8% (95% CI: 0.05–0.12) and the 85% (95% CI: 0.78–0.9) of the patients were steroid free. The recurrence rates were the least in the retroperitoneoscopic group 1% (95% CI: 0–0.04) and Conn's syndrome group 2% (95% CI: 0.01–0.05) and highest in open group 15% (95% CI: 0.07–0.28) and Pheochromocytoma group 10% (95% CI: 0.07–0.16). Steroid independence rates were best in the Conn's syndrome group 97% (95% CI: 0.85–0.99) and laparoscopic group 88% (95% CI: 0.75–0.95). **Conclusions:** Partial adrenalectomy can obviate the need for steroid replacement in the majority of patients and local recurrence rates appear to be infrequent. For patients with hereditary and bilateral adrenal tumours, partial adrenalectomy should be recommended as a primary surgical approach whenever possible.

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1. Introduction

Partial adrenalectomy was proposed by Walz [1], using minimally-invasive retroperitoneal approach, attaining good results in terms of surgical outcome, preserve the cortical function and avoid life-long steroid replacement. The risk of Addisonian crisis can occur in up to 10–35% of patients post bilateral

adrenalectomy, even with adequate steroid therapy [2], and in case of more frequent small functioning tumours (sporadic pheochromocytomas, aldosterone or cortisol producing adenomas), emphasizing the benefits of this procedure that allows to save the normal adrenal tissue, and to minimize the risk of future adrenal failure in case of contralateral gland surgery [3,4]. Since the introduction of partial adrenalectomy, several studies have been published trying to address the issue standard approach of performing the total adrenalectomy most of these being retrospective studies. We sought to evaluate the recurrence and functional outcomes of Cortical-sparing adrenalectomy by performing a meta-analysis of the literature published till date.

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2. Methods

2.1. Study protocol

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses PRISMA guidelines where possible in performing our systematic review [5]. We performed a systematic search through MEDLINE (from 1950), PubMed (from 1946), EMBASE (from 1949), Current Contents Connect (from 1998), Cochrane library, Google scholar, Science Direct, and Web of Science to February, 2015. The search terms included “partial adrenalectomy, subtotal adrenalectomy and cortical-sparing adrenalectomy” which were searched as text word and as exploded medical subject headings where possible. No language restrictions were used in either the search or study selection. The reference lists of relevant articles were also searched for appropriate studies. A search for unpublished literature was not performed.

2.2. Study selection

We included studies that met the following inclusion criteria:

1. Studies identifying the population of patients with an adrenal tumour who underwent partial adrenalectomy; and
2. Original data reporting the outcomes of patients undergoing partial adrenalectomy.

2.3. Data extraction

We performed the data extraction using a standardized data extraction form, collecting information on the publication year, number of cases, total sample size, country and clinical data. The procedures were classified into open, laparoscopic, retroperitoneoscopic and tumours were categorized into Conn's syndrome, pheochromocytoma and non pheochromocytoma (non-functioning adrenal tumour, adrenal metastases and others). The outcomes were also measured by the site of the procedure. The pooled event rates and 95% confidence intervals were calculated.

2.4. Statistical analysis

Pooled event rates and 95% confidence intervals were calculated for recurrence and steroid supplementation using a random effects model [6]. We tested heterogeneity with Cochran's Q statistic, with $P < 0.10$ indicating heterogeneity, and quantified the degree of heterogeneity using the I^2 statistic, which represents the percentage of the total variability across studies which is due to heterogeneity. I^2 values of 25, 50 and 75% corresponded to low, moderate and high degrees of heterogeneity respectively [7]. We quantified publication bias using the Egger's regression model [8], with the effect of bias assessed using the fail-safe number method. The fail-safe number was the number of studies that we would need to have missed for our observed result to be nullified to statistical non-significance at the $p < 0.05$ level. Publication bias is generally regarded as a concern if the fail-safe number is less than $5n + 10$, with n being the number of studies included in the meta-analysis [9]. All analyses were performed with Comprehensive Meta-analysis (version 2.0).

3. Results

The original search strategy retrieved 507 studies. The abstracts were reviewed and after applying the inclusion and exclusion criteria, articles were selected for full-text evaluation. Of the

articles selected, only 60 met full criteria for analysis and are summarised in Table 1. The years of publication ranged from 1998 to 2014.

3.1. Event rates

The overall recurrence rate was 8% (95% CI: 0.05–0.12) and the 85% (95% CI: 0.78–0.9) of the patients were steroid free. The recurrence rates were the least in the retroperitoneoscopic 1% (95% CI: 0–0.04), Conn's syndrome 2% (95% CI: 0.01–0.05) and highest in open 15% (95% CI: 0.07–0.28) and Pheochromocytoma group 10% (95% CI: 0.07–0.16). As far steroid independence is concerned, rates were best in the Conn's syndrome cluster 97% (95% CI: 0.85–0.99) and laparoscopic cohort 88% (95% CI: 0.75–0.95). The event rate and confidence intervals are depicted in Table 2

3.2. Heterogeneity and publication bias

The heterogeneity of outcomes has been summarized in Table 2 and Table 3. The reason for significant heterogeneity may be attributed to different population groups, No publication bias was detected using the Egger's regression model.

4. Discussion

The objective of this review was to evaluate the tumour recurrence and steroid sparing effect of partial adrenalectomy. The adverse side effects commonly encountered with chronic steroid dependence, have led surgeons to adopt an adrenal sparing procedure in patients with adrenal tumours. While too little steroid replacement can lead to Addisonian crisis and death, too much is associated with premature osteoporosis, complications of hypertension and diabetes. Other common side effects include: mood changes, diarrhoea, abdominal distension, nausea, dyspepsia, increased appetite, peptic ulcers, adrenal suppression, candidiasis, hirsutism, increased intraocular pressure, immunosuppression, hypertension, oedema, and hypokalaemia [10–12].

The amount of residual adrenal cortical tissue to be left in situ in order to maintain an acceptable cortical function while ensuring adequate tumour clearance has been debated. Most authors suggest a margin of at least 3–5 mm is necessary to attain good results [13–15]. However, there is no definitive data regarding the amount of tissue needed to preserve and maintain physiological adrenal function.

Preservation of the adrenal vein ensures that the adrenal remnant will drain to the circulation. Roukounakis et al., [15] the vein-preservation technique ensures a functioning stump, provides better haemostasis due to adequate drainage avoiding congestion of the gland, omits a time-consuming and potentially hazardous step of the operation, and finally gland mobilization allows application of a vascular stapler, reducing operation time. However, some authors advocate division of the vein but careful preservation of the minor venous plexuses of the retroperitoneal space instead [16,17].

Fu et al. [18] was a randomized trial comparing retroperitoneoscopic partial versus total adrenalectomy for aldosterone producing adenoma demonstrating a shorter operative time with partial adrenalectomy but this did not attain statistical significance. However, the intraoperative blood loss in the partial adrenalectomy group was significantly higher than in the total adrenalectomy group. A decreased dose of or fewer antihypertensive were prescribed at final follow-up in the partial adrenalectomy cohort.

On the other hand, Ishidoya et al. [19] recommended total laparoscopic adrenalectomy in patients over partial adrenalectomy with unilateral aldosterone producing adenoma and primary

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