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Peer Review File

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Comment 1: First, I do not think the abstract is informative. Please briefly explain the purpose of this review and the clinical needs for this review. The authors should have some specific comments on the indications and technical aspects of laparoscopic transperitoneal adrenalectomy in the abstract.

Reply 1: I agree. The abstract has been rewritten to better reflect the content and include important technical information.

Changes in the text: Popularised in the early 1990s, transperitoneal laparoscopic adrenalectomy (TLA) has become a standard surgical approach for most adrenal pathology, apart from invasive adrenal cancer. Factors such as reduced blood loss, less post-operative pain and shorter length of hospital stay have confirmed its superiority over open surgery. Pre-operative considerations regarding the tumour (size, risk of malignancy, whether it is functioning), the patient (presence of obesity, previous abdominal surgery, comorbidities) and the surgeon (caseload, access to wider MDT support from radiology and endocrinology) govern the choice of TLA when managing a patient with adrenal disease. In general, TLA is indicated for radiologically benign functioning tumours up to around 10cm, indeterminate non-functioning tumours up to 6cm in the absence of suspicious radiology, and adrenal metastasectomy provided the tumour is organ-confined. Cortex-sparing, subtotal adrenalectomy may be an option in patients with inherited phaeochromocytoma. Radiologically diagnosed adreno-cortical carcinoma is a specific contra-indication to TLA, particularly if there is evidence of local invasion; extensive adhesions may be a relative contraindication. Bilateral tumours may be approached with sequential right and then left TLA, but if they are both <5cm, retroperitoneoscopic adrenalectomy is also an option. In experienced hands TLA is very safe with a reported mortality of less than 1% but morbidity is seen in up to 10%. Low surgical volume is associated with poorer outcomes such as related-readmission and conversion to open surgery. Pitfalls such as missed-diagnosis of

functioning tumours, wrong site surgery, failure to diagnose local invasion pre-operatively, and post-operative complications are minimised by access to an experienced core MDT (endocrinologists, radiologists, oncologists and pathologists trained in the management of adrenal disease), contemporaneous radiology, adequate caseload, and regular reporting of surgical outcomes via National Registries. Improvements in care will continue to accrue from concerted efforts to concentrate adrenal surgery in centres with appropriate personnel and expertise.

Comment 2: Second, in the main text, the authors may consider to use a figure or table to briefly show indications and technical aspects of laparoscopic transperitoneal adrenalectomy.

Reply 2: The author agree and Table 1 has been added to summarise some technical tips and pitfall
Changes in the text: See Table 1

Comment 3: In the conclusion part, challenges in the implications and possible research focuses in relation to the technique are also needed.

Reply 3: text has been added to reflect where future progress could be made eg robotics and centralisation

Changes: 'To conclude, adrenalectomy is a relatively uncommon operation with a clear volume-outcome relationship, especially in the setting of very rare pathology such as phaeochromocytoma and adrenal cancer. As with other complex surgical procedures, there is a clear case for centralisation of adrenal surgery into regional hubs with access to an experienced wider multi-disciplinary team. Continued focus on this will lead to better patient outcomes in the future. It remains to be demonstrated, but advances in technology, such as robotic surgery, may have a role to play in expanding indications and improving surgical outcomes for minimally invasive adrenalectomy.'