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7 **Evolution of Minimally Invasive Adrenal Surgery at a Tertiary Care Centre**  
8 **in Oman**

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15  
16 **Abstract**

17 **Objective:** We reviewed the case records of adrenalectomy cases at our institution between  
18 January 2010 and December 2020 and report the outcomes of both open and laparoscopic  
19 adrenalectomy (LA). **Methods:** This retrospective study included patients who underwent  
20 adrenal surgery from January 2010 to December 2020. We recorded demographic details,  
21 indications, surgical approach, intra operative data and complications. The final pathology and  
22 outcome at the last follow up was also documented. Data was analyzed through the SPSS  
23 program. **Results:** Fifty two patients underwent 61 adrenalectomy procedures. Six patients had  
24 bilateral procedure and 3 patients underwent redo surgery accounting for 55 subjects. Open  
25 adrenalectomy (OA) was performed on 11 patients and 44 patients underwent LA. Majority of  
26 the patients (27) were obese having BMI > 30. Functional adenoma was excised in 36 patients  
27 with final diagnosis of Conn's syndrome in 15, Pheochromocytoma in 13 and Cushing syndrome  
28 in 9 patients. Five patients had surgery for oncological indications. Nonfunctional adenoma was  
29 excised in 13 patients, with a mean size of 8.9 cm (range 4-15 cm). The mean duration of surgery  
30 was less in laparoscopic procedure (199 min) compared to open (246 min). The mean estimated

31 blood loss in LA was significantly less (108ml vs 450 ml, p-value < 0.05). Out of 55 subjects  
32 only 1 patients developed Clavien-dindo grade 2 complication. **Conclusion:** At our institution  
33 both laparoscopic and open adrenalectomy were safely performed. There is a trend to perform  
34 LA and with experience the duration of surgery and EBL are demonstrating positive trend.

35 **Keywords:** Adrenal Gland Surgery; Laparoscopic Adrenalectomy; Open Adrenalectomy;  
36 Pheochromocytoma; Adrenal Metastasis; Nonfunctional Adrenal Tumors; Oman.

### 37 38 **Advances in Knowledge**

- 39 • This study looks at the transition of adrenal surgery from open approach to minimally  
40 invasive approach at our center.
- 41 • It provides objective evidence that adrenal surgery is feasible in Oman.
- 42 • This study demonstrates that laparoscopic adrenalectomy is being performed with good  
43 results comparable to any other good center in the world.

### 44 **Application to Patient Care**

- 45 • Adrenal gland is located in a difficult to access location and required large surgical incision.  
46 Laparoscopic surgery for adrenal gland has the unique advantage of providing excellent  
47 exposure without large incision. The advancements in surgical techniques for  
48 adrenalectomy and the results of laparoscopic adrenalectomy at our center provide an  
49 opportunity for our patients to benefit.
- 50 • This study shows that less blood loss, operative time and better cosmetic results of  
51 laparoscopic adrenalectomy make it the standard of care for most patient requiring adrenal  
52 surgery
- 53 • The complication rate is well within internationally acceptable range

### 54 55 **Introduction**

56 Laparoscopic adrenalectomy (LA) is now recognized as the gold standard approach for adrenal  
57 pathology. The post-operative analgesics requirements, hospital stay, surgical morbidity and better  
58 cosmetic results are the main driving forces.<sup>1, 2, 3</sup> LA was first described by Ganger et al in 1992  
59 for Cushing disease, since then the list of indications have now expanded to include almost all  
60 benign and malignant adrenal neoplasms.<sup>4</sup> The growing experience and systematic training  
61 programs have resulted in marked reduction in the duration of surgery and morbidity.<sup>5</sup> In this study

62 we reviewed our 10-years' experience of open and transperitoneal laparoscopic adrenalectomy  
63 procedures at our institution. To our knowledge this is the first large case series from Oman  
64 comparing the open and laparoscopic approach for adrenalectomy.

65

## 66 **Methods**

67 Ethics review committee approval was obtained from our institution to conduct a retrospective  
68 chart review of all the adult patients undergoing adrenal surgery our institution. Ten-year period  
69 from January 2010 to December 2020 was selected and using electronic medical record (EMR) of  
70 the hospital information system (Trakcare® United health care systems) we identified 55 eligible  
71 subjects.

72

73 Collected data included patient demographic features, comorbidities, Body mass index (BMI),  
74 preoperative diagnosis, intraoperative details including surgical approach (Open/Laparoscopic),  
75 duration of surgery, estimated blood loss, pathological diagnosis. The post-operative  
76 complications were also recorded and graded according to Clavien-Dindo classification system.  
77 Data was analyzed using SPSS program version 21.0. The analysis was done using variable graph,  
78 pie-chart and frequency tables. Frequency tables provides information about mean, median and  
79 standard deviation. A p-value of  $<0.05$  was considered as statistically significant.

80

## 81 **Results**

82 Fifty two patients underwent 61 adrenalectomy procedures. Six patients had bilateral procedure  
83 and 3 patients underwent redo surgery accounting for 55 subjects. Open adrenalectomy (OA) was  
84 performed on 11 patients and 44 patients underwent LA. There were 13 male and 39 female  
85 patients. The mean age was 44 years (range 15-70 years).

86

87 Majority of the patients (36) underwent adrenalectomy for functional tumors. Five patients had  
88 surgery for oncological indication including two for metastasis from other organs. The frequency  
89 of distribution of final diagnosis is illustrated in Fig1.

90

91 The median tumor size was slightly larger in the open surgery group (5 cm vs. 6.5 cm). The details  
92 of difference in size are illustrated in Table 1. Nonfunctional adenoma was excised in 13 patients,  
93 with a mean size of 8.9 cm (range 4-15 cm).

94

95 ASA 2 was the most common category in 63% patients. Majority of the patient were obese with  
96 52% having BMI  $\geq$  30, the frequency of American society of anesthesia (ASA) score and BMI  
97 groups is shown in the Figure 2.

98

99 Laparoscopic adrenalectomy was performed in 44 patients and 11 underwent open adrenalectomy.  
100 The mean duration of open surgery was 246 min (median 241 min) vs. 189 min (median 197 min)  
101 in the laparoscopic group. In patient undergoing open surgery the estimated mean blood loss (EBL)  
102 was 450 ml (100 to 1000 ml) vs. 108 ml (range 50 ml to 500 ml) in the laparoscopic group (p=0.05).  
103 We also independently analyzed the unilateral adrenalectomy group and found similar trend. The  
104 mean duration of surgery and EBL in unilateral laparoscopic vs. unilateral open adrenalectomy  
105 were 198 min vs. 248 min and 108 ml vs. 245 ml respectively.

106

107 We used operating time as a surrogate maker to reflect the surgical expertise. After January 2017,  
108 we transitioned to a subspecialty based approach and all adrenal procedures were referred to  
109 urology service having a lead surgeon with dedicated interest in adrenal surgery. To assess the  
110 impact of this intervention we created two groups, Time period 1(before December 2017) and  
111 Time period 2 (after January 2017). We found that the mean duration of surgery reduced from  
112 mean of 206 min to 145 min only.

113

114 There were no complications in majority of patients. One patient developed diarrhea related to  
115 clostridium infection and 3 patients developed paralytic ileus (2 in open and 1 in laparoscopic  
116 group). The frequency of complications according Clavien-Dindo system of classification of  
117 surgical complications is shown in Table 2.

118

119 Three patient were treated for recurrence of disease. Two of them belong to a family with von  
120 hippel-lindau (VHL) abnormality where the recurrence is not unexpected over a period of time. In

121 one patient there was a suspicion of cancer on the histopathology and the patient underwent  
122 revision LA with free margins and is doing well after 4 years of follow up.

123

## 124 **Discussion**

125 Adrenal surgery for a functional tumor like Cushing's disease and Pheochromocytoma is  
126 exceptionally rewarding in terms of the physiological outcomes. The additional benefits of  
127 minimally invasive approach in terms of cosmetics, minimal blood loss, lesser analgesic  
128 requirement, hospital stay and higher patient satisfaction have certainly placed laparoscopic  
129 adrenalectomy (LA) at the pedestal of gold standard.<sup>6, 7, 8</sup> In this study we looked at the safety and  
130 efficacy of intraperitoneal laparoscopic adrenalectomy at our institution and how it has evolved to  
131 be now a routine surgical procedure.

132

133 Functional adrenal tumors present multiple challenges in the peri operative period. Significant  
134 number of patients are also obese. In our study 52% of our patients had BMI of  $\geq 30$ , which is well  
135 known to be associated with intraoperative difficulties.<sup>9, 10</sup> Secondary hypertension is also one of  
136 the common presentation of adrenal tumors. Studies have shown that almost two third of the  
137 indications of surgery are for functional tumors exhibiting hypertension.<sup>11</sup> In our study 67%  
138 patients had secondary hypertension related to either Cushing disease, Pheochromocytoma or  
139 Conn's disease. Post operatively all patients were successfully weaned off the antihypertensive  
140 medications.

141

142 The evolution of laparoscopic adrenal surgery has witnessed an expansion of indications.  
143 Functional tumors like Pheochromocytoma which were initially regarded as out of bound are now  
144 routinely treated by key-hole surgery.<sup>12</sup> In our series we successfully performed LA on 13 patient  
145 with Pheochromocytoma. Laparoscopic treatment of conditions like adrenocortical neoplasm has  
146 also been reported with comparable oncologic outcome.<sup>13</sup> We performed LA in 3 cases of primary  
147 adrenocortical neoplasm with adequate surgical margins and acceptable oncologic control.  
148 Adrenalectomy for metastatic disease is increasing performed and can be considered as standard  
149 of care for some cancers with solitary adrenal metastasis.<sup>14</sup> We performed laparoscopic  
150 metastatectomy in 2 patients with adrenal metastasis. One of them relapsed within one year but  
151 the other patient has no evidence of disease with more than 3 years of follow up. The limit of size

152 of the gland to undergo LA has always been debatable and some authorities have recommended  
153 the upper limit as  $> 6\text{cm}$ .<sup>15</sup> Technical difficulty and suspicion of malignancy are regarded as factors  
154 responsible to cap the size limit.<sup>16</sup> In our study we have performed LA for tumors up to 15 cms  
155 with no significant increase in operating time or blood loss. In these cases we did not encounter  
156 any incidental finding of cancer, in our opinion the advancements in radiology have increased our  
157 confidence. Modern CT scan and MRI of the adrenal gland using specific protocols now have  
158 excellent ability to predict the final pathology.<sup>17</sup> In our cohort of LA for non-functional adenoma  
159 the mean size of the gland removed was 5.8cm.

160  
161 In our series the LA had also retained the advantage of shorter operative time with the mean  
162 duration of LA as 189 min compared to open adrenalectomy with the mean of 246 min. The EBL  
163 in LA is significantly less with the mean of 170ml comparing with 450ml in open procedure, with  
164 the significant p-value  $< 0.001$ .

165  
166 We also looked a two time periods for LA, before December 2017 and after January 2017. This  
167 division was created to assess the impact of change in the referral system at our institution as from  
168 January 2017 onwards all cases of adrenal tumor were referred to a team dedicated to do LA. We  
169 found that the mean duration of surgery reduced from 206 min to 145 min. We must acknowledge  
170 the limitation here as the cases were not controlled for complexity of procedure.

171  
172 The overall rate of complications of adrenalectomy, both open and laparoscopic was very low at  
173 our institution. Majority of patients did not have any complications. Out of 55 subjects one  
174 developed grade 2 Clavien-Dindo complications. There we no grade 3 or above complications.  
175 During follow up 3 patients had disease recurrence and underwent redo surgery. Two of them  
176 belonged to a family of patients with VHL abnormality and were predisposed to high risk of  
177 recurrence. One patient had suspicious pathology for adrenocortical cancer and had revision  
178 surgery.

## 179 180 **Conclusion**

181 Both laparoscopic and open adrenalectomy have been performed safely at our institution with low  
182 morbidity. The benefits of minimally invasive approach clearly favor laparoscopic approach

183 especially in term of duration of surgery and estimated blood loss. However in selected cases there  
184 is still a role of open approach.

185

### 186 **Authors' Contribution**

187 NA and KMS designed the study. NA, MSM and YS collected the data. NA, MSM, GB and  
188 KMS performed the statistical analysis. NA and MSM drafted the manuscript. GB, OE and KMS  
189 critically reviewed the manuscript and revised the manuscript. All authors approved the final  
190 version of the manuscript.

191

### 192 **Conflict of Interest**

193 The authors declare no conflicts of interest.

194

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197

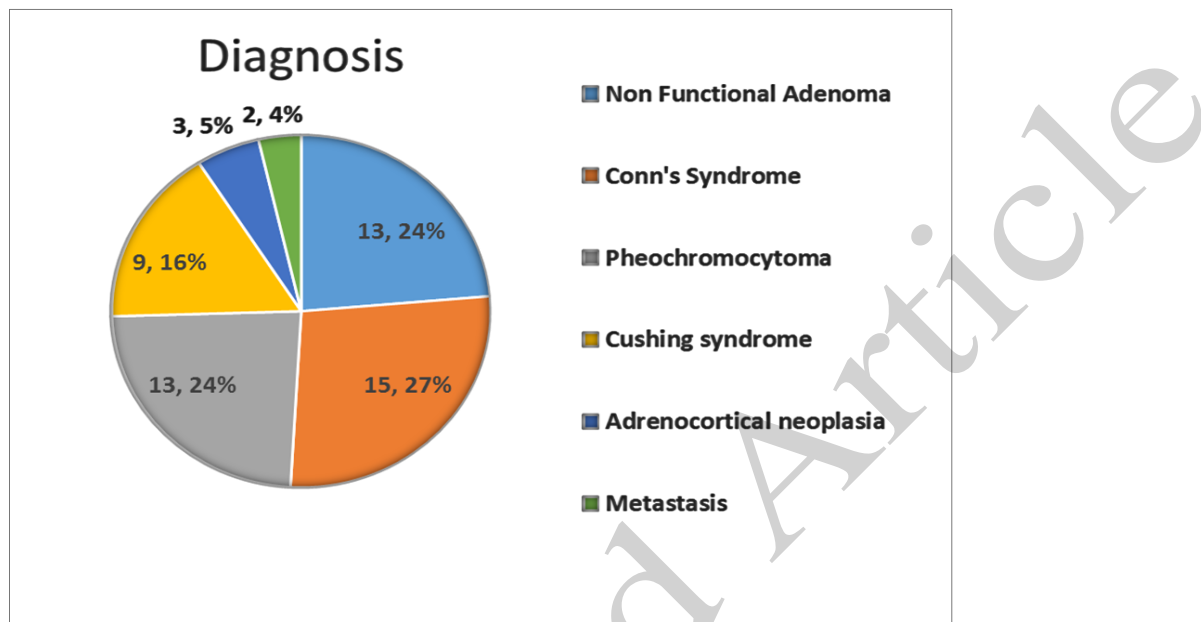
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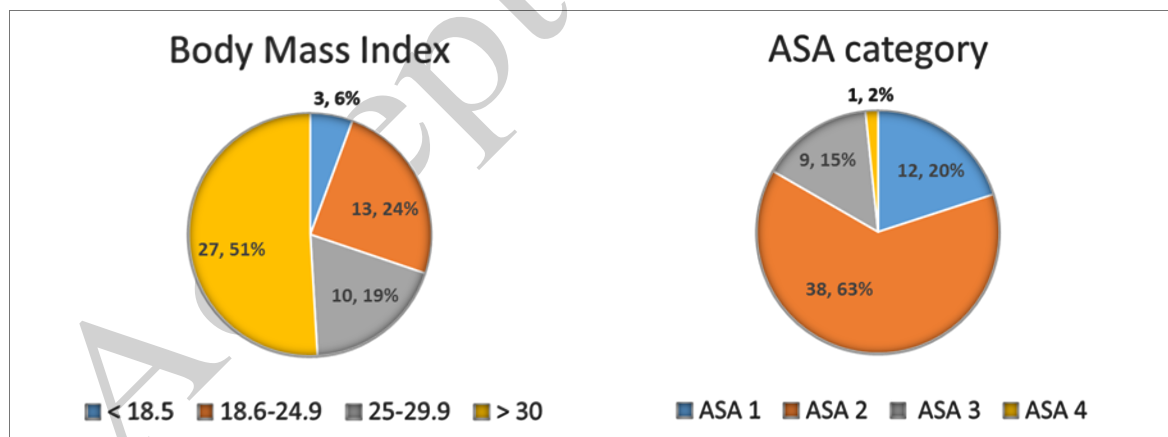


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244



245 **Figure 1:** The Distribution of Frequency of Diagnosis for Adrenalectomy  
246

247



248 **Figure 2:** The Distribution of Body Mass Index (BMI) and American Society of  
249 Anesthesiologist (ASA) of the Patients undergoing Adrenalectomy  
250

251 **Table 1:** The distribution of tumor size in the two groups

|                    | Laparoscopic<br>Adrenalectomy<br>N=44 | Open<br>Adrenalectomy<br>N=11 |
|--------------------|---------------------------------------|-------------------------------|
| Mean size in cm    | 5.8                                   | 6.8                           |
| Median size in cm  | 5                                     | 6.5                           |
| Range              | 1.5-15                                | 3.8-11                        |
| Standard deviation | 3.49                                  | 2.22                          |

252  
253 **Table 2:** The frequency of surgical complications in the two groups

| Clavien-Dindo<br>Grade | Total<br>N=55 | Laparoscopic<br>Adrenalectomy | Open<br>Adrenalectomy |
|------------------------|---------------|-------------------------------|-----------------------|
| 0                      | 51            | 0                             | 0                     |
| 1                      | 3             | 1                             | 2                     |
| 2                      | 1             | 1                             | 0                     |
| 3                      | 0             | 0                             | 0                     |

254