

The role of laparoscopic resection of metastases to adrenal glands

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Background: The potential role of the laparoscopic approach for metastases to the adrenal gland is debated. We review here a series of patients consecutively submitted to laparoscopic adrenalectomy (LA) for suspected adrenal metastasis (AM).

Methods: Retrospective study (consecutive series) of LA for AM. We measured parameters associated to primary tumor and metastasis. Statistical analysis: stepwise regression model.

Results: Thirty-seven LA were performed on 36 patients. The mean age was 62.1 yrs. The side was right in 13 cases. Primary tumor was in the lung (n=22), breast (n=4), colon-rectum (n=4), kidney (n=3), thyroid, melanoma and ovary (n=1 each). Thirty-three out of 37 were confirmed to be AM (mean diameter 50 mm). Twenty-five were single metastasis. One LA was converted due to cava vein infiltration. Mean operative time was 142 min', median p.o. hospital stay was 3 days. After a mean follow-up of 33 months, 9 patients (25%) were alive free of disease, 6 (17%) were alive with disease. Mean post-adrenalectomy DFI was 19 months (range, 0–97 months), and it was the most predictive variable for survival (P<0.001).

Conclusions: The dimensions and absence of invasion on imaging, the evolutive status of the disease and the performance status of the patient are key factors for LA, which is associated with adequate oncologic results, a quicker postoperative recovery, and potential survival benefits.

Keywords: Adrenal tumor; adrenal metastasis (AM); laparoscopic adrenalectomy (LA); oncologic surgery; minimally invasive surgery

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Introduction

Adrenalectomy for metastatic disease can be indicated in various oncological settings (from diagnosis to cure). Since the first description in 1982 (1), several reports describe prolonged survival after open adrenalectomy for isolated metastasis, and some refer its feasibility by minimally invasive approach, with the related advantages and acceptable oncologic results (2). Nonetheless there is still debate about the opportunity to treat this dreaded disease by a laparoscopic approach. Furthermore, there is some uncertainty about which patient to submit to surgery with a curative intent, since factors predictive of prolonged

survival have not been clearly identified.

In this study we review a series of patients consecutively submitted to laparoscopic adrenalectomy (LA) for suspected/proven adrenal metastasis (AM) in a tertiary referral centre, with the aim to verify the appropriateness of the laparoscopic approach for the removal of metastases to the adrenal glands (and to identify those factors that may eventually affect survival).

Methods

Retrospective study on a series of subjects consecutively referred for surgical removal of a suspected AM during

the period 2001–2010 at the Department of General Surgery, S. Chiara Hospital, University of Pisa. The aim of surgery was the *en bloc* removal of the adrenal gland with the surrounding fatty tissue to achieve complete local control of the disease. We evaluated several preoperative and perioperative details (related to the patient, the primary tumor, the AM, the operative technique and the pathology report). The metastasis is defined as “synchronous” if detected at diagnosis of primary tumour or less than 6 months later, “metachronous” if detected after 6 months or more from the diagnosis.

Follow-up consisted in contacting the patient and/or the referring oncologist and registering the clinical and instrumental data. Data were analysed on an intention-to-treat basis. We report details on overall postoperative course, and an analysis of survival-associated variables among the cases with a histologically confirmed metastasis.

Statistical analysis

We first correlated all the measured variables with the status of the patient (alive/dead) by a univariate analysis, which showed that the factor mostly correlated to survival was post-adrenalectomy disease free interval (DFI) ($P < 0.01$). We then employed a semi-rigid mathematical model (multivariate analysis—stepwise regression and a backward procedure) where the status of the patient (alive/dead) was the dependent variable, and the size of the metastasis, preoperative DFI and post-adrenalectomy DFI were the independent ones. Statistics were performed by Stat-view software, and P values of < 0.05 were considered significant.

An informed consent was obtained before the operation while a written consent to enter the study is not needed since it is retrospective.

Results

During the 10 years' observation period, 37 adrenalectomies for metastases were performed on 36 patients. All patients underwent a LA (the approach was lateral transperitoneal). There were 23 males and 13 females, the mean age was 62.1 yrs (SD 8.8); the right adrenal was involved in 13 cases, the left in 24 (1 patient had bilateral involvement). The primary tumor was in the lung ($n=22$), breast ($n=5$), colon-rectum ($n=4$), kidney ($n=3$), then thyroid, melanoma and ovary ($n=1$). 12 lesions were synchronous, 25 metachronous (median DFI before detection of AM: 20 months). Of the

37 removed specimens, 33 were metastases (with a mean diameter of 50 mm, SD 25, range 14–120), 3 were benign masses (in patients with lung, breast and kidney primary), and 1 adrenal was normal (the 30 mm lump was actually on the outer aspect of the gastric fundus in a patient with an ocular melanoma). Twenty-five lesions were considered isolated metastasis, while 12 were multiple (other metastatic sites were present in personal medical history, but under control at operation). All interventions but one were completed laparoscopically. One patient with a resected NSCLC had a 50 mm adrenal mass with an intraoperative doubt of cava vein infiltration, so was converted to open surgery; the metastasis was removed *en bloc* with part of the cava vein. Overall, the adrenalectomy was radical (R0) in 32 cases, and apparently radical in one (micro-invasion of margins, R1); in another case the adrenal was removed with the surrounding soft tissue with a *no touch* technique, but the palpation of the retired specimen didn't reveal any nodule, so we re-explored the area (also with the help of intraoperative laparoscopic US) and discovered a 30 mm lump (melanoma metastasis) on the gastric fundus. A few days later, after a proper discussion, the patient was submitted to gastric resection.

The mean operative time was 142 min' (range 75–250 min'). Intraoperative complications: a micro-laceration of the spleen managed laparoscopically by topic haemostatics. Postoperative morbidity: a dyspnoea in a pneumectomized patient which required an ICU management; and a postoperative cholecystitis in the only patient converted to open surgery. Median postoperative hospital stay was 3 days (range 2–22 days).

After a mean follow-up of 33 months (range 4–84 months), 9 patients (25%) were alive free of disease, 6 (17%) were alive with disease, 17 (47%) were dead and 4 (11%) were lost to follow-up. No signs of port recurrence and no local (operative site) recurrence were recorded according to referring oncologists (we had personal access only to part of re-staging images).

The overall measured median survival was 26 months and the mean post-adrenalectomy DFI was 19 months (range 0–97 months). The mean follow-up of alive patients was 45 months.

The mathematical model introduced with the stepwise regression (backward procedure) considering the three chosen independent variables together (diameter of the metastasis and pre-adrenalectomy DFI, suggested by the literature as independent factors of prolonged survival (3–5), and post-adrenalectomy DFI, individuated by the

univariate analysis as the factor mostly related to survival in our sample) was not significant ($P=n.s.$). Then at step 1 the model excluded the less significant variable (diameter of the metastasis), and the new p value for the remaining two was: $P=0.04$. Finally, the most predictive, single variable for survival was post-adrenalectomy DFI ($P<0.001$).

Discussion

The management of the primary tumor and of its metastases is a complex task which is best dealt with a multidisciplinary approach. The frequency of the discovery of an adrenal mass in oncologic population is continuously rising due to the intensive use of highly sensible imaging techniques in the evaluation of the disease burden. The indication for surgical removal of an AM with curative intent classically consisted in the isolated AM (3-23) but there is some agreement that also oligometastatic patients in whom all tumoral foci seem amenable to complete resection or control should be included (4). Obviously, there are also other factors to take into account when deciding how to manage a patient with AM, in particular the evolutive status of the disease, that is its biologic aggressiveness, and the performance status of the patient. Therefore a multispecialty team evaluation is essential to plan effective management strategies. The first step is the confirmation or the exclusion of the diagnosis of AM: in the recent years the combination of high resolution CT and PET scans has proved to be very accurate in distinguishing benign from malignant adrenal masses (13,24); the use of FNAC is rarely needed in indeterminate cases (25). Notwithstanding the reliability of pre-operative imaging in excluding the benign nature of the mass, a basic functional evaluation is warranted, especially in order to exclude pheochromocytoma (8,26), perhaps essential also if the treatment choice is radiofrequency ablation of the mass (27,28).

Over the last decade, LA has been proposed also for the treatment of AM (9) and, despite initial concerns regarding less than optimal oncologic efficacy (port site metastases, local recurrence), it is slowly gaining acceptance. When compared to open adrenalectomy, LA for AM results in less morbidity (including pain), shorter hospital stay, quicker recovery and better cosmetic results (that is all the benefits of laparoscopic approach), with the same oncologic outcomes (2,5,26,29,30).

Our series confirms, on a consistent number of patients

affected by different primaries, which the laparoscopic approach can be applied in most cases of AM, and should be preferred to a traditional open approach. We observed a very low morbidity, a shorter hospital stay than with an open approach, a quicker return to normal activities, these two being widely demonstrated advantages of the laparoscopic operation. The skills acquired with the increasing practice of laparoscopic procedures even in the domain of oncology for other intra-abdominal organs together with the development of technologically advanced instruments, like the ultrasonic dissectors, has currently elevated the LA as the preferred initial option for the treatment of AM, provided that signs of extra-adrenal invasion are excluded/controlled, and that the surgeon is confident and skilled enough with this technique. Our oncologic results (at a mean follow up of nearly 3 years) are similar to those reported in the literature, in term of quality of resection and survival. None of the parameters we measured was identified as an independent predictor of prolonged survival but post-adrenalectomy DFI. Survival is a direct expression of the tumor biology and response to systemic therapy. In case of residual, subclinical tumor after LA, the less it is aggressive, the longer will be the postoperative DFI and the overall survival.

The details of operative technique are of utmost importance to achieve a successful result, in that an incomplete resection is a cause of compromised survival (3,7). The limits of the dissection are the kidney, the diaphragmatic pilasters, the quadratus lumborum muscle, the cava vein on the right side, the pancreatic tail on the left. All the adrenal-containing cellular tissue should be cleared-off these structures *en bloc*. If this objective cannot be met, then the conversion to a traditional open adrenalectomy should be immediate.

In conclusion, this report adds to the accumulating evidence that the resection of AM, when the disease is amenable to complete treatment, offers survival benefits (31). The size of the AM, the absence of extra-adrenal invasion on imaging, the biology of the disease and the performance status of the patient are the key factors that should indicate its surgical removal by a laparoscopic approach, which is today the first surgical option. A properly performed, radical LA is usually associated with good oncologic results (in term of local relapse), a quick postoperative course, and potential benefits on overall survival.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the Azienda Ospedaliero-Universitaria Pisana committee (Prot. n° 14064). An informed consent was obtained before the operation while a written consent to enter the study is not needed since it is retrospective.

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