Surgery ■■ (2017) ■■–■■

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/ymsy

American Association of Endocrine Surgeons

Metabolic syndrome is associated with increased postoperative complications and use of hospital resources in patients undergoing laparoscopic adrenalectomy

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ARTICLE INFO

Article history:
Accepted 13 June 2017

Background. Rates of obesity and metabolic syndrome continue to rise worldwide; however, the impact of metabolic syndrome on outcomes following adrenalectomy has not been described. In this study, we sought to investigate the effects of metabolic syndrome on postoperative 30-day morbidity, mortality, and utilization of hospital resources in a large cohort of patients undergoing elective laparoscopic adrenalectomy.

Methods. Patients who underwent laparoscopic adrenalectomy from 2005 to 2014 were identified in the American College of Surgeons National Surgical Quality Improvement Program database. Patients with body mass index ≥30 kg/m^2 who also had diabetes and hypertension requiring medications were defined as having metabolic syndrome. Univariate and multivariable analyses were performed for the outcomes of 30-day mortality/morbidity, major complications, and utilization of hospital resources (prolonged duration of stay ≥3 days and requirement for perioperative blood transfusion).

Results. Of the 3,502 patients included in the study, 395 had metabolic syndrome (11.3%). Patients with metabolic syndrome were older ($P < .001$) and had a greater percentage of preoperative comorbidities ($P < .05$) than patients without metabolic syndrome. On unadjusted analysis, metabolic syndrome was associated with an increased risk for mortality/morbidity, major complications, duration of stay, operative time, and risk for blood transfusion (all $P < .001$). On multivariable analysis, metabolic syndrome was an independent predictor of overall mortality/morbidity (odds ratio, 1.86; $P < .001$), major complications (odds ratio, 1.99; $P < .001$), pulmonary complications (odds ratio, 1.83; $P = .049$), the need for blood transfusion (odds ratio, 1.94; $P = .04$), and prolonged length of stay (odds ratio odds ratio, 1.34; $P = .02$).

Conclusion. The presence of metabolic syndrome increased the risk for postoperative complications after laparoscopic adrenalectomy and was associated with 2-fold risk for blood transfusion and 34% increased odds of a prolonged hospital stay.

Rates of obesity and metabolic syndrome (MetS) continue to rise to epidemic levels worldwide. MetS is believed to affect around a quarter of the US population, with an estimate of >50 million adults meeting the criteria for diagnosis.[1,2] Although several definitions of MetS exist,[3,4] these criteria generally encompass a constellation of insulin resistance and hyperglycemia, dyslipidemia, hypertension, and abdominal obesity. Patients with MetS are at increased risk for developing cardiovascular and metabolic disorders, including stroke, coronary artery disease, chronic kidney disease, peripheral vascular disease, and type 2 diabetes.[5]

Increasing evidence supports the association of adrenal pathology with MetS through the effects of excess adrenal hormones on various metabolic pathways.[6] Cushing's syndrome shares many of the diagnostic features of MetS, and it has been postulated that hypercortisolism contributes to the pathogenesis of both states.[7] This is supported by the variable degree of hypothalamic–pituitary–adrenal axis hyperactivity and increased peripheral cortisol activity seen in patients with MetS.[8] A similar association has been shown in patients with subclinical cortisol-secreting adrenal incidentalomas[6] and, paradoxically, even in those with apparently nonfunctioning adenomas,[9] suggesting that "silent" hormonal dysfunction may lead to an adverse cardiometabolic profile. An alternative theory is that

Presented at the 38th Annual Meeting of the American Association of Endocrine Surgeons, Orlando, FL, April 2–4, 2017.

Sources of financial support: none.

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https://doi.org/10.1016/j.surg.2017.06.023
0039-6060/

adrenal incidentalomas are an unrecognized manifestation of MetS, arising as a consequence of sustained hyperinsulinemia,[10] in a mechanism similar to insulin-mediated ovarian stimulation in polycystic ovary syndrome. Studies have also shown a higher prevalence of MetS among patients with primary aldosteronism, an effect thought to be due to the blood pressure–independent effects of aldosterone on glucose metabolism and endothelial dysfunction.[11]

The presence of MetS has been shown to adversely affect perioperative outcomes after various general operations, including hepatectomy,[12] pancreatectomy,[13] gastric bypass,[14] and colorectal resections.[15] However, the impact of MetS on outcomes after adrenalectomy has not yet been described. We hypothesize that patients with MetS who undergo adrenalectomy have worse surgical outcomes than those without MetS. Hence, the objective of this study was to evaluate the effect of MetS on 30-day postoperative morbidity, mortality, and utilization of hospital resources in a large multicenter cohort of patients who underwent laparoscopic adrenalectomy. Patient information was taken from American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database.

Methods

Data source

This study was conducted as a retrospective analysis of the ACS-NSQIP database from 2005 through 2014. ACS-NSQIP is a prospective, nationally validated database that collects information on 135 variables including preoperative risk factors, intraoperative variables, and 30-day postoperative morbidity and mortality in patients undergoing major surgery at >500 participating hospitals of varying size and academic affiliation. Trained surgical reviewers collect deidentified data from medical records. Specific details regarding data collection, outcome variable definitions, quality control, and personnel training are described elsewhere.[16] The Institutional Review Board of the Mayo Clinic (Rochester, MN) has deemed the analysis of ACS-NSQIP data exempt from review. The ACS-NSQIP and the hospitals participating in the ACS-NSQIP are the source of the data used herein; they have not been verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Study participants

The ACS-NSQIP participant user file was reviewed for all patients ≥18 years of age who underwent laparoscopic adrenalectomy for nonmalignant adrenal disease between 2005 and 2014 using the Current Procedure Terminology (CPT) code 60650. As laparoscopy is currently the predominant surgical approach in treating adrenal disease, we chose not to include patients who underwent an initial open adrenalectomy (CPT 60540 or 60545) or surgery for adrenocortical carcinoma based on the assumption that these patients required a more complex operation and would have different anticipated outcomes. However, the need for conversion from a laparoscopic to an open procedure was recorded if the CPT code for open adrenalectomy also appeared under the same anesthetic as the laparoscopic adrenalectomy. Postoperative diagnosis was categorized according to the International Classification of Diseases, 9th edition (ICD-9) diagnostic codes as follows: "Cushing's syndrome" (255.0), "pheochromocytoma" (255.6), "hyperaldosteronism" (255.1, 255.10, and 255.12), and "benign non-functioning adenoma" (227.0). The ICD-9 codes for "unspecified disorder of the adrenal glands" (255.9) and "other specified disorders of adrenal glands" (255.8) were grouped together in an "other" category. Patients who underwent laparoscopic adrenalectomy for other indications were not included in this study.

Exclusion criteria from the cohort included any of the following preoperative conditions: emergent operation; American Society of Anesthesiologists (ASA) class V; ventilator dependence; sepsis; septic shock; systemic inflammatory response syndrome; pneumonia; acute renal failure; preoperative transfusion >4 units of blood; dialysis; coma; and open wound, wound infection, or both. Patients who underwent concurrent operations that were outside the reasonable range of expected procedures performed during elective laparoscopic adrenalectomy were excluded to minimize the confounding effects of these procedures on outcomes. Further exclusions included patients with unknown body mass index (BMI) as MetS could not be determined without this variable. Our algorithm for patient selection is detailed in Figure.

The preoperative characteristics studied included age, sex, race, BMI, and ASA class. Comorbidities included obesity, diabetes mellitus (on oral hypoglycemic medications or insulin), hypertension, smoking status, alcohol use, severe chronic obstructive pulmonary disease (COPD), dyspnea with moderate exertion or at rest, chronic steroid use, any cardiac disease (including congestive heart failure, history of myocardial infarction 6 months before surgery, previous percutaneous coronary intervention, previous cardiac surgery, or history of angina within 30 days of operation), and any vascular disease (including history of revascularization or amputation for peripheral vascular disease, rest pain/gangrene, history of transient ischemic attacks, or cerebrovascular accident with neurologic deficit within 30 days of operation). Current alcohol use, all variables included in "any cardiac disease" except congestive heart failure, and all variables included in "any vascular disease" were phased out of ACS-NSQIP between 2011 and 2012; for these comorbidities, univariate analysis was limited to patients for whom data were available through 2012.

Exposure of interest

MetS was defined using a modification of the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria[3] as the presence of obesity (BMI ≥30 kg/m^2), diabetes (both insulin and noninsulin dependent), and hypertension. This definition has been used by other studies in the literature evaluating the impact of MetS on surgical outcomes[12,13,17] and accounts for the absence of waist circumference and lipid profile in the ACS-NSQIP database.

Outcomes of interest

Primary outcomes of interest were 30-day mortality, overall mortality/morbidity, and any serious complication. Overall morbidity occurrences of interest included cardiac complications (acute myocardial infarction or cardiac arrest), pulmonary complications (pneumonia, pulmonary embolism, unplanned intubation, or ventilator dependence), renal complications (acute renal failure, progressive renal insufficiency, or urinary tract infection), neurologic complications (cerebrovascular accident, coma lasting >24 hours, or peripheral nerve injury), septic complications (sepsis or septic shock), wound complications (wound dehiscence or superficial, deep, or organ space surgical site infections), bleeding complications (requirement for blood transfusion), and deep venous thrombosis (DVT). A major complication was defined as any of the complications just listed, excluding superficial surgical site infection, urinary tract infection, and peripheral nerve injury.

Secondary outcomes were related to utilization of hospital resources and included length of stay (LOS) from operation to discharge, total time spent in the operating room (OR), receipt of any blood transfusion, unplanned readmission, and return to the OR within 30 days. Prolonged LOS was defined as duration of hospitalization of ≥3 days. Any blood transfusion was defined as at least

Please cite this article in press as: Omair A. Shariq, et al., Metabolic syndrome is associated with increased postoperative complications and use of hospital resources in patients undergoing laparoscopic adrenalectomy, Surgery (2017), doi: 10.1016/j.surg.2017.06.023