Peptides 60 (2014) 8–12

Contents lists available at ScienceDirect

Peptides

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

Elevated plasma visfatin levels correlate with conversion of laparoscopic cholecystectomy to open surgery in acute cholecystitis

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ARTICLE INFO

Article history:
Received 11 July 2014
Received in revised form 19 July 2014
Accepted 21 July 2014
Available online 31 July 2014

Keywords:
Visfatin
Acute cholecystitis
Conversion
Laparoscopic cholecystectomy
Open surgery

ABSTRACT

Visfatin correlates with inflammation and its levels in peripheral blood are associated with some inflammatory diseases. This study aimed to assess the relationship between plasma visfatin levels and conversion of laparoscopic cholecystectomy to open surgery in acute cholecystitis. One hundred and forty-six acute cholecystitis patients and 146 sex- and age-matched healthy controls were recruited and their plasma visfatin levels were determined using an enzyme immunoassay. 17 patients (11.6%) underwent conversion. Plasma visfatin levels were statistically significantly elevated in all patients (97.2 ± 41.8 ng/mL), those with (161.4 ± 71.3 ng/mL) or without conversion (88.7 ± 26.9 ng/mL), compared to controls (40.3 ± 13.3 ng/mL, all $P < 0.001$). A linear regression analysis showed that plasma visfatin levels were positively associated with plasma C-reactive protein levels ($t = 0.510$, $P < 0.001$). A logistic-regression analysis showed that age [odds ratio (OR) 1.160, 95% confidence interval (CI) 1.011–1.332, $P = 0.035$] and plasma visfatin levels (OR 1.035, 95% CI 1.005–1.066, $P = 0.022$) appeared to be the independent predictors of conversion. A receiver operating characteristic curve analysis found that plasma visfatin levels predicted conversion with high area under curve (AUC) (AUC, 850; 95% CI, 0.781–0.903). The AUC of the visfatin concentration was similar to that of age (AUC, 0.738; 95% CI, 0.659–0.807) ($P = 0.188$). Visfatin improved the AUC of age to 0.914 (95% CI, 0.856–0.954) ($P = 0.011$) using a combined logistic-regression model. Thus, high plasma levels of visfatin are associated with systemic inflammation, and may independently predict conversion of laparoscopic cholecystectomy to open surgery in acute cholecystitis.

Introduction

Acute cholecystitis is the most frequent complication arising from gallstones [30,31]. Laparoscopic cholecystectomy (LC) has proved to be a "revolutionary" transformation in gallbladder surgery [22,24]. Given the numerous advantages presented by it, LC is considered the "gold standard" in treating gallstones [8,23]. LC for acute cholecystitis is associated with a higher conversion rate compared to elective surgery and a higher rate of postoperative complications due to inflammatory changes [10,11]. Preoperative identification of operative difficulties predictors is particularly important in non referential LC centers and in the hospitals in which open cholecystectomy became a rarity as a primary prevention in intraoperative injuries of the bile ducts and vascular structures. Systemic inflammatory response has been suggested as pathogenic factors of acute cholecystitis [27]. Thus, inflammatory markers may have potential to predict conversion of LC to open surgery in acute cholecystitis.

Visfatin is an adipokine identified in 2004 and thus named for the suggestion that it would be predominantly produced and secreted in visceral fat [5]. Visfatin is highly preserved across animal evolution and has a molecular weight of 52 kDa with 491 aminoacids [25]. It is identical to pre-B cell colony-enhancing factor, described in 1994 as a cytokine produced by lymphocytes, acting on lymphocyte maturation and inflammatory regulation [13,21]. Visfatin was also soon recognized as the formerly described Nicotinamide phosphoribosyltransferase, the limiting enzyme in nicotinamide adenine dinucleotide biosynthesis [7]. Recent studies have shown that visfatin is closely related to immune processes and

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http://dx.doi.org/10.1016/j.peptides.2014.07.017
0196-9781/

is a major proinflammatory cytokine in a variety of inflammatory processes [2,12,28].

Visfatin has been identified as an acute phase adipocytokine [28]. A more recent study has shown that significantly increased serum levels of visfatin detected in the early period after abdominal surgery preceded increase in the levels of other proinflammatory markers including tumor necrosis factor-alpha, interleukin-6, and C-reactive protein; and therefore, visfatin could serve as an early predictor of the development of inflammatory changes in patients undergoing surgery [32]. At present, there is a paucity of data available on circulating plasma visfatin concentrations in patients with acute cholecystitis. Thus, we sought to determine visfatin in plasma of patients with acute cholecystitis and to further investigate the ability of plasma visfatin to predict conversion of LC to open surgery in acute cholecystitis.

Materials and methods

Study population

This study prospectively included acute cholecystitis patients undergoing three-incision LC from The Yinzhou Second People's Hospital between May 2010 and December 2013. Non-selection criteria involved previous or current malignant diagnoses, history of upper abdominal surgery, other infectious, organic, endocrine or systemic abnormalities, missing of follow-up, unavailable blood sample, refusal of participation and incomplete clinical information. The acute cholecystitis is defined as acute pain in the right upper quadrant of the abdomen that lasts longer than 3 h and requires an urgent admittance and is accompanied with cholelithiasis, leukocytosis > 10×10^9/L, body temperature > 37.5 °C, a positive Murphy's sign and ultrasonographic signs – thickened gallbladder wall, edematous gallbladder wall, or pericholecystic fluid collection [29]. Healthy age- and sex-matched volunteers were recruited as control group. At study entrance, all participants or their legal representatives gave their informed consent, and study protocol was approved by the Ethics Committee of The Yinzhou Second People's Hospital before implementation.

Clinical assessment

The recorded information included age, sex, diabetes mellitus, duration of symptoms, body temperature, operative risk according to American Society of Anesthesiologist score (ASA), laboratory results (C-reactive protein, white blood cell count, erythrocyte sedimentation rate, blood glucose level), and ultrasonographic parameters (pericholecystic fluid collection, adhesion of the gallbladder, impacted stone of cystic duct, gallbladder wall thickness). A patient was considered converted, if for any reason, the planned laparoscopic procedure was abandoned and open conventional cholecystectomy was resorted to.

Operative technique

The standard technique was used for all laparoscopic cholecystectomies. First, a 10-mm port was inserted in the subumbilical region under vision, followed by two 5-mm lateral ports. Dissection of the Calot's triangle was done either using a hook or a Maryland forceps. Cystic duct and artery were defined and clipped separately and divided. Gallbladder removal from the liver bed was accomplished by using monopolar electrocautery and extracted through the epigastric port. When conversion was required, either a Kocher's incision or an upper midline incision was made. Decision for conversion was based on surgeon's clinical judgment. All laparoscopic cholecystectomies were performed by experienced surgeons.

Determination of plasma visfatin levels

The informed consents were obtained from all participants or their legal representatives before the blood were collected. Venous blood samples were collected prior to surgery for the patients and at the physical examination day for the healthy volunteers. Venous blood samples were placed on ice. After centrifugation ($1500 \times g$ for 20 min), plasma samples were stored at −70 °C until assayed. Plasma visfatin levels were measured using a commercial enzyme immunoassay kit (Phoenix Pharmaceuticals, Belmont, Calif.) according to manufacturer's instructions. All samples were assayed in duplicate. The person carrying out the assays was completely blinded to the clinical information.

Statistical analysis

Statistical analysis was performed with SPSS 19.0 (SPSS Inc., Chicago, IL, USA) and MedCalc 9.6.4.0 (MedCalc Software, Mariakerke, Belgium). All values are expressed as mean ± standard deviation or counts (percentage) unless otherwise specified. Differences between groups were assessed for statistical significance using chi-square test, Fisher exact test or Student's t test when appropriate. The associations of plasma visfatin levels with other variables were analyzed by Spearman's or Pearson's correlation coefficient and followed by a multivariate linear regression. The relation of visfatin to conversion was assessed in a logistic-regression model with odds ratio (OR) and 95% confidence interval (CI). The receiver operating characteristic (ROC) curves were used to determine the best threshold of visfatin values to predict conversion with calculated area under curve (AUC). In a combined logistic-regression model, the additive benefit of visfatin to age was estimated. A P value of <0.05 was considered significant for all test.

Results

Study population characteristics

Initially, 167 patients with acute cholecystitis were evaluated. 21 patients were excluded because of the following reasons. 3 patients had malignant diagnoses; 4 patients, history of upper abdominal surgery; 2 patients, severe pneumonia; 2 patients, renal failure; 3 patients, dexamethasone within 2 weeks; 3 patients, unavailable blood samples; 2 patients, refusal of participation; 2 patients, incomplete clinical information. Finally, one hundred and forty-six (87.4%) acute cholecystitis patients were assessed and 146 sex- and age-matched healthy controls were recruited. This group of patients included 63 males and 83 females, aged 22–80 years with a mean age of 57.6 ± 18.0 years. 30 (20.6%) patients had diabetes mellitus. The mean duration of symptoms was 2.3 ± 1.6 days (0–8 days). 72 (49.3%) patients had body temperature >38 °C. 60 patients had ASA I; 61 patients, ASA II; 23 patients, ASA III; 2 patients, ASA IV. The mean plasma-sampling time was 3.7 ± 1.9 days (1–9 days); the mean white blood cell count, $17.0 \pm 6.3 \times 10^9$/L ($10.2–36.0 \times 10^9$/L); the mean erythrocyte sedimentation rate, 30.0 ± 13.2 mm/h (8–78 mm/h); the mean blood glucose level, 12.1 ± 4.4 mmol/L (4.0–31.0 mmol/L); the mean plasma C-reactive protein level, 66.0 ± 44.3 mg/L (9.9–184.5 mg/L). 32 (21.9%) patients had pericholecystic fluid collection; 51 (34.9%) patients, adhesion of the gallbladder; 48 (32.9%) patients, impacted stone of cystic duct; 62 (42.5%) patients, gallbladder wall thickness >4 mm.