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Association between misty mesentery with baseline or new diagnosis of cancer: a matched cohort study

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ABSTRACT

We compared the prevalence of a baseline diagnosis of cancer in patients with and without misty mesentery (MM) and determined its association with the development of a new cancer. This was a retrospective, HIPAA-compliant, IRB-approved case-control study of 148 cases and 4:1 age- and gender-matched controls. Statistical tests included chi-square, *t*-test, hazard models, and C-statistic. Patients with MM were less likely to have cancer at baseline (RR = 0.74, $p = 0.003$), but more likely to develop a new malignancy on follow-up (RR = 2.13, $p = 0.003$; survival analysis HR 1.74, $p = 0.05$). MM may confer an increased probability of later developing cancer, particularly genitourinary tumors.

1. Introduction

Radiological studies often report many incidental findings, some of which require follow up. However, ordering CT follow up can cause more harm than benefit, particularly in the cases of pseudodisease, due to cost, radiation exposure, and overdiagnosis. Thus, it is important to determine, in an evidence-based manner, which incidental findings warrant follow-up. In 1996, Mindelzun et al. coined the term misty mesentery to describe the CT finding of an increase in the density of the mesenteric fat due to the infiltration of inflammatory cells, fluid, tumor, and fibrosis, which is often associated with mass effect and central lymph nodes (Fig. 1) [1]. Although mentioning several causes, such as mesenteric panniculitis, they stated that non-Hodgkin's lymphoma was the most common cause of its isolated presentation. Since then other authors have also suggested this and associations of misty mesentery with other malignancies. Because of these reports, it has become a relatively common practice among radiologists to describe the presence of an isolated misty mesentery as a nonspecific finding that could be associated with cancer, therefore deserving further evaluation, although this is not a universally accepted conclusion. Several other studies, such as those by Nakatani et al. [2] or Seo et al. [3] also seemed to find an association with cancer. However, several other studies have found contradictory results, such as those reported by Gögebakan et al. [4], Halligan et al. [5], or Protin-Catteay et al. [6], which did not find any statistically significant risk increase of cancer in misty mesentery.

Due to this limited contradictory data on the significance of misty mesentery, we undertook a retrospective matched cohort study to compare the prevalence of a known diagnosis of cancer in patients with and without misty mesentery at baseline imaging, and to determine its association with the development of a new diagnosis of cancer.

2. Material and methods

This was a retrospective, HIPAA compliant, IRB approved study of adult patients with and without misty mesentery on CT scans acquired between January 1, 2000 and December 31, 2010.

2.1. Computerized data collection

One author (REDACTED) performed all data collection and created a database for analyses. We first identified patients with misty mesentery (cases). In our institution, the minimum criteria to characterize a misty mesentery are 1) an increase in the density of the fat surrounding the mesenteric vessels, compared to the retroperitoneal and/or subcutaneous fat, and 2) the presence of borderline enlargement of mesenteric lymph nodes (Fig. 1). We did not use any short axis size threshold, as these are not typically reliable to determine the presence or absence of disease; instead, we compared the size of lymph nodes within the area of misty mesentery to other mesenteric lymph nodes. We used Montage (Montage Healthcare Solutions, Philadelphia, PA) to

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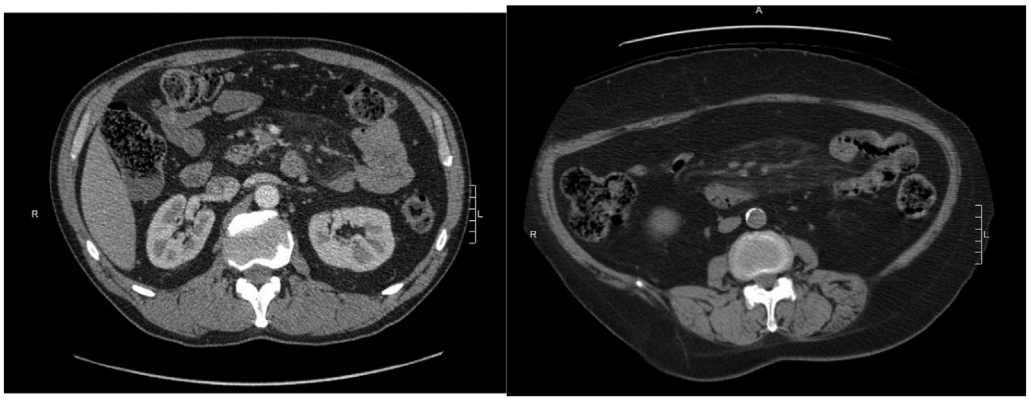

Fig. 1. Misty Mesentery examples. Characteristic mesenteric fat stranding, lymphadenopathy, "fat ring sign", and capsule formation can be seen.

search our radiology information system (RIS) database for CT scan reports of the abdomen or abdomen/pelvis (with or without contrast) that included keywords associated with misty mesentery. The following keywords were utilized: misty OR mesenteritis OR panniculitis. Multiple scans of the same patient were identified and excluded. Finally, a single author (REDACTED) individually confirmed the presence of misty mesentery on the scan. Misty Mesentery was further classified by severity (on a scale of 1 to 4, 4 being most severe) based on the presence/absence of lymphadenopathy, the presence/absence of a capsule, and the severity of the hazy appearance of the mesentery. All scans were reviewed and if the patient had prior CT scans, those images were examined to identify the first study, within our study time frame, on which the mesenteric findings became apparent, in case they had been present previously and not reported. Misty mesentery was an incidental finding in these CT scans for different indications, rather than representing the reason for the CT scan.

Next, 4:1 age- and gender-matched controls, i.e. patients without misty mesentery, were identified for each case. Age was broken down into the following categories: 18–39 years, 40–49 years, 50–59 years, 60–69 years, 70–79 years, and ≥ 80 years. To increase feasibility, we used a systematic random sample to identify controls. We selected the two patients scanned immediately before and the two patients scanned immediately after the case-patient, matched for age and gender, were included in the study. Patients whose scans were in the picture archiving and communication system (PACS) for storage only with no report available were excluded. One author (REDACTED) performed a quality control and independently reviewed the all images of the control population to confirm the true absence of misty mesentery.

In addition to age and gender, two authors (REDACTED) reviewed and extracted the following data from the medical records: date of CT scan, use of iodinated intravenous contrast, number of post contrast scan phases (single versus multiphase), patient-care setting (inpatient, outpatient, or emergency department), baseline nonmalignant diagnoses, history of malignancy known at the time or identified on the CT scan, subsequent diagnosis of malignancy (and type), as well as date of the new diagnosis or last encounter if no malignancy was diagnosed. Malignant diagnoses included any primary malignancy or metastatic disease. These diagnoses were identified in the list of problems, history and physical examination notes, progress notes, and/or pathological reports. Baseline nonmalignant diagnoses were categorized utilizing six ICD-9 groups: diseases of the circulatory system, chronic liver disease and cirrhosis, chronic kidney disease, chronic obstructive pulmonary disease, tobacco use disorder, and diabetes mellitus.

2.2. Statistical methods

We used Pearson's chi-square test to compare the proportions of a) contrast enhanced computed tomography (CECT) scans, b) multiphase CECT scans, c) known diagnosis of malignancy prior to or at the time of CT scan, and d) new diagnosis of malignancy in patients with and without misty mesentery. The test was also used to assess for differences in the distribution of patient origin (emergency department, hospitalized patient, or ambulatory care). The mean follow-up time of patients with and without misty mesentery was compared using the two-sample Student's *t*-test.

A Cox proportional hazard model was used to determine if misty mesentery is associated with the diagnosis of new cancer (failure). This analysis included only those patients who did not yet have a diagnosis of cancer at baseline. Two models were used: 1) an unadjusted model, and 2) a multivariate analysis. In the multivariate analysis, we controlled for patient-care setting and the use of CT scan contrast protocol, as these were seen to be different at baseline. We tested the assumption of proportionality of all variables by including time-dependent covariates to the model. The starting point for time to failure was the date of the initial CT scan that identified the misty mesentery. We censored the follow-up time at the date of last known appointment if a patient did not develop cancer during the study time frame.

Statistical analysis was performed using the STATA® Data Analysis and Statistical software version 12 (StataCorp, College Station, TX). An alpha level of 0.05 was considered to indicate statistical significance.

3. Results

3.1. Population characteristics

We identified 252 examinations using the search keywords. Of those, 80 scans represented multiple examinations for the same patient and only the earliest study showing misty mesentery was included. A further 19 patients were excluded after the images were evaluated and the findings were determined to represent a mesenteric abnormality not fitting a misty mesentery; for example, focal inflammatory changes adjacent to diverticulitis. An additional 5 patients were excluded after the review of prior examinations showed misty mesentery present prior January 1, 2000, as the search software was unable to search before the year 2000 to find controls. After appropriate exclusions, our sample consisted of 148 patients with misty mesentery (60 women, 40.5%: 88 men, 59.5%) and 600 patients without it (236 women, 39.3%: 364 men, 60.7%) (Fig. 2). The mean age of patients were 63.5 years (standard deviation = 13.9) and 61.9 years (standard deviation = 14.4) for patients with and without misty mesentery, respectively. As populations were matched, there was no difference in gender or age between populations. No statistically significant difference in any non-malignant diagnosis was seen upon follow up.

76.4% of patients with misty mesentery were scanned in an outpatient facility, compared to 65.2% of control patients ($p = 0.009$). On the contrary, the proportion of patients with misty mesentery scanned in an outpatient setting was smaller than the proportion of controls (12.8% vs. 22%, $p = 0.013$). No differences were seen in the proportions of scans acquired in the emergency department (12.8%, 19/154 vs. 10.8%, $p = 0.51$). Intravenous contrast was used with similar