Increased Incidence of Endoscopic Erosive Esophagitis in Solid Organ Transplant Recipients

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Background/Aims: Solid organ transplant recipients frequently report gastrointestinal symptoms, especially heartburn or dyspepsia. However, the prevalence of endoscopic erosive esophagitis (EE) and associated risk factors after transplantation are unknown. The aim of this study was to determine whether there was a high incidence of endoscopic findings of EE in solid organ transplant recipients. Methods: This retrospective case-control study included 256 of 3,152 solid organ transplant recipients who underwent sequential screening upper endoscopic examinations and an equal number of controls. Results: Forty-four (17.2%) and 16 (6.2%) cases of EE were detected in the solid organ transplant and control groups, respectively (p<0.001). In the multivariate analysis, transplantation was significantly associated with EE (odds ratio [OR], 6.48; 95% confidence interval, 2.74 to 15.35). Factors such as old age (OR, 1.17), the presence of a hiatal hernia (OR, 5.84), an increased duration of immunosuppression (OR, 1.07), and the maintenance administration of mycophenolate mofetil (OR, 4.13) were independently associated with the occurrence of EE in the solid organ transplant recipients. Conclusions: A significant increase in the incidence of endoscopically detected EE was observed in solid organ transplant recipients. This increased incidence was associated with the type and duration of the immunosuppressive therapy. (Gut Liver 2012;6:349-354)

Key Words: Transplantation; Erosive esophagitis; Gastroesophageal reflux; Mycophenolate mofetil; Barrett esophagus

INTRODUCTION

According to literature, cancer is expected to surpass cardiovascular complications as the primary cause of death in transplanted patients within the next 2 decades. A nationwide cohort study from Sweden indicated a 3-fold increased risk of de novo tumors after solid organ transplantation (SOT). In addition, increased incidence of de novo esophageal cancer in the population of liver transplant recipients has been reported. Accumulating evidence suggests that gastric acid is the major factor in the pathogenesis of gastroesophageal reflux disease and its complications, including erosive esophagitis (EE), Barrett’s esophagus (BE), and esophageal adenocarcinoma. In the case of BE, which is recognized as a complication of EE and a pre-malignant condition that may lead to the development of esophageal adenocarcinoma, the proximal level of the squamocolumnar junction no longer coincides with the gastroesophageal junction.

Gastrointestinal complications are frequent in SOT recipients and may involve any segment of the gastrointestinal tract. These disorders may be related to stress, infections, or exacerbation of pre-existing gastrointestinal pathology. In addition, immunosuppressive agents may cause gastrointestinal side effects, either directly or by favoring the development of bacterial or viral infection. Severe gastrointestinal disorders may develop in approximately 10% of SOT patients, eventually leading to graft loss and even patient death. Gastrointestinal complications may also result in reduction of the dose of immunosuppressant drugs and associated risk of organ rejection. According to various studies of patient-reported gastrointestinal symptoms, the majority of patients complained of symptoms such as indigestion, abdominal pain, constipation, diarrhea, or reflux. In particular, symptoms indicating the possibility of gastroesophageal reflux disease (heartburn or regurgitation) were reported to occur in 17% to 43% of renal transplant recipients during the post-transplant period. Similarly, it was reported that incidence of
such symptoms rose from 3.4% to 27.6% after living donor liver transplantation.\textsuperscript{17,18} From these results, we hypothesized that a considerable number of transplant recipients are likely to show endoscopic evidence of EE or BE after transplantation. However, to date, no study using endoscopy to screen for EE in SOT recipients, compared to a general non-transplant population, has been performed, and little is known regarding the occurrence of BE after organ transplantation. Indeed, a majority of investigations include endoscopic examination only for individuals with serious symptoms.\textsuperscript{14,15} Furthermore, there appears to be more interest in infectious than non-infectious esophagitis in SOT recipients. To overcome these limitations, it will be essential to evaluate the endoscopic findings of the gastroesophageal junction by using upper endoscopy as a screening tool for the population undergoing SOT.

The aim of the current study was to determine whether the incidence of endoscopic findings of EE or BE is high in SOT recipients compared with a control population.

**MATERIALS AND METHODS**

1. **Patients**

We performed a case-control study at the Severance Hospital in Seoul, Korea from 2005 to 2010. The study population consisted of subjects who had pre and post-transplant upper gastrointestinal endoscopy among 3,152 SOT (kidney, liver, pancreas, or heart transplantation) recipients. Patients were excluded for the following reasons: no baseline endoscopic examination prior to SOT (n=1,941), no data of follow-up endoscopy after transplantation (n=409), diagnosed of EE or BE in baseline endoscopy (n=133), previous gastric cancer or colorectal cancer (n=21), previous gastric surgery (n=9), high-risk symptoms such as occult blood, anemia, hematemesis, hematochezia, melena, vomiting, dysphagia, odynophagia, palpable mass, jaundice, or weight loss (n=70), current use of nonsteroidal anti-inflammatory drugs (NSAIDs) or other ulcerogenic agents (n=99), or drug history of acid suppressive treatment within 6 months from 2nd endoscopic examination (n=214). The control group consisted of age- and gender matched patients who had undergone sequential endoscopies at intervals over 1 year as part of a health check-up during the same period and who had no endoscopically observed EE or BE in the first endoscopy. SOT patients (n=256), including 164 kidney, 85 liver, 5 pancreas, and 2 heart recipients, were selected using the procedure illustrated in Fig. 1. Patients in an age- and gender-matched screening population (n=256) were enrolled as controls. Both the groups consisted of 141 men (55.1%) and 115 women (44.9%); their mean age was 47.3±6.9 years.

2. **Endoscopic findings**

Our hospital operates a digital filing system for endoscopic images. All digital endoscopic images were independently and retrospectively reviewed by two trained endoscopists to investigate the endoscopic findings, including hiatal hernia, EE, and BE. If any inconsistency in the assessment of the digital endoscopic images occurred, a final diagnosis was decided upon by a joint review of the digital endoscopic images.

3. **Hiatal hernia**

Hiatal hernia was diagnosed when the distance between the gastroesophageal junction and the diaphragmatic hiatus was 1 cm or more.\textsuperscript{20}

4. **EE**

EE was diagnosed based on the Los Angeles Classification and was divided into three groups: none, mild (grades A and B), or severe (grades C and D).\textsuperscript{21}

5. **BE**

The presence of BE was diagnosed based on the C&M criteria.