Introduction
Capsule endoscopy (CE) represents a significant advance in the investigation of small bowel disease. The diagnostic power of CE continues to improve while its scope of use has expanded to include evaluation of obscure gastrointestinal bleeding (OGIB), Crohn disease, intestinal tumors, polyposis, and other small bowel diseases\(^1\)\(^-\)\(^5\).

Among various small bowel diagnoses, angiodysplastic lesions of the small bowel were more accurately identified compared with other pathologies\(^6\). Angiodysplastic lesions are the most common cause of OGIB, accounting for about 30–40% of lesions. Unfortunately, there is a lack of comprehensive epidemiologic studies...
for OGIB in the elderly. This study reports the risk factors of OGIB with CE in the elderly.

Materials and Methods

A retrospective study was performed on 152 patients who underwent CE between March 2004 and November 2008. Clinical and other data were collected and evaluated retrospectively. Patients without OGIB and patients whose examination did not reach the cecum capsule were excluded. The patient flow chart is summarized in Table 1. All patients had undergone at least one upper endoscopy and colonoscopy prior to performance of CE. All the patients signed the informed consent.

To analyze possible risk factors for angiodysplasia in the elderly, we systematically assessed several potential risk factors: (1) chronic liver disease; (2) past medical history of heart disease; (3) diabetes mellitus; (4) pulmonary disease; and (5) chronic renal disease.

CE procedure

After an overnight fast of 12 hours, all patients swallowed the CE. Patients were allowed to drink 2 hours after ingesting the capsule and to eat a light meal 4 hours later. Patients were free to leave the endoscopy department, with instructions to return about 7–8 hours after ingestion to have the recorder disconnected. The recorded information was downloaded into the computer, and images from the stomach and the small bowel were analyzed using the RAPID 3 software (Given Imaging Ltd., Yoqneam, Israel). The intestinal transit time was calculated from the first view of duodenum until the cecum was reached. The study was regarded as “positive” when at least one highly relevant lesion was found (P2), “negative” when the abnormality found could not explain blood loss (P1), or when no abnormality (P0) was seen.

Statistical analysis

Comparisons between categorical measures were carried out using $\chi^2$ test using the phi correlation for an index between nominal variables. To identify possible factors associated with angiodysplastic lesion, all possible factors were examined by a binary logistic regression analysis. Odds ratio and corresponding 95% confidence intervals were generated for all variables. A $p$ value < 0.05 was regarded as statistically significant. SPSS 13.0 (SPSS Inc., Chicago, IL, USA) for Windows was used in all statistical analyses.

Results

In total, 152 CE studies were reviewed. Of these, 121 studies were used in the statistical analysis after exclusions were made, as shown in Table 1. The mean age of the patients was 57.9 years (range, 13–89 years; 41.3% women). Using CE, the most commonly detected bleeding sources or clues in the small bowel included angiodysplasias (red flat mucosal lesions with visible borders), active bleeding (fresh blood localization without definite lesion identified), ulcers (an interruption of the mucosa with visible depth) and tumors (Figure). Angiodysplastic lesions found in small intestine are listed by age distribution in Table 2. When stratified

<table>
<thead>
<tr>
<th>Table 1. Patient flow chart</th>
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<tr>
<td>Patient pool (152 patients considered for the study)</td>
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<tr>
<td>Excluded: 12 patients without obscure gastrointestinal bleeding found clinically</td>
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<td>Excluded: 10 patients with short duration of capsule batteries</td>
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<td>Excluded: 9 patients with capsule not reaching the cecum</td>
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<tr>
<th>Table 2. Angiodysplastic and non-angiodysplastic lesions in small intestine by age distribution</th>
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<tbody>
<tr>
<td>Age ≥ 65 years</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Lesion, n (%)</td>
</tr>
<tr>
<td>Angiodysplastic</td>
</tr>
<tr>
<td>Non-angiodysplastic</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Figure. Positive findings for 121 patients undergoing capsule endoscopy.
according to age, the occurrence of angiodysplastic lesions was 52% in the older population and 25% in the younger population ($p < 0.01$).

Results of binary logistic regression analysis for all cases investigated revealed possible risk factors for angiodysplastic lesions (Table 3). The main factor associated with angiodysplastic lesions was increased age ($\geq 65$ years). Because aortic stenosis is a known risk factor for angiodysplasia, we analyzed whether a past medical history of heart disease was a risk factor for angiodysplasia. These patients did not have an increased risk for angiodysplasia (odds ratio, 0.83; 95% confidence interval, 0.20–3.48; $p = 0.80$), and neither did patients with chronic renal disease (odds ratio, 2.47; 95% confidence interval, 0.70–8.71; $p = 0.16$).

### Discussion

The number of people older than 65 years constitutes a substantial and growing proportion of the population in Taiwan11. Worldwide, the number of persons older than 65 years will approach 750 million by 205012. Old age, primarily because of associated comorbidity, may dramatically influence the prognosis of some gastrointestinal diseases, such as gastrointestinal bleeding13. Unfortunately, because of age-related changes in pain perception, the clinical manifestations of these disorders may be atypical and variable, resulting in a delayed diagnosis.

OGIB could be subclassified as obscure-overt bleeding, defined as recurrent passage of visible blood, and obscure-occult bleeding, defined as recurrent iron deficiency anemia and/or recurrent positive fecal occult blood test results14,15. The common causes of OGIB are vascular lesions, ulceration, small bowel tumors, and jejunal diverticulosis16,17. The diagnostic yield of CE for the suspected bleeding source in patients with OGIB has been reported to range from 38% to 93%18. The small bowel is the most likely source of bleeding in patients with continuing blood loss and negative upper and lower gastrointestinal endoscopies. This tumor location is particularly true in patients <50 years, in whom small bowel mass lesions are most frequently diagnosed19. Alternative methods for evaluating the small bowel include balloon-assisted enteroscopy, angiography, radionuclide imaging, enteroclysis, computed tomography, and magnetic resonance enterography. Their diagnostic yield depends on several factors, such as availability, clinical condition, and the experience of the interpreter. In elderly patients, it may be difficult to obtain many of these studies in a noninvasive manner.

Angiodysplastic lesions are the most frequent cause of OGIB. Individuals with large and numerous angiodysplastic lesions had higher transfusion requirements, lower hemoglobin levels, higher rebleeding rates, and a higher proportion of therapeutic procedures performed after CE20. Although an endoscopic classification for vascular lesions of the small bowel has been established18, their cause is unknown and the result of a degenerative process associated with aging is probable. Junquera et al.21 proposed that incremental vascular endothelial growth factor expression appears to play a pathogenic role in the development of colonic angiodysplasia. Angiodysplasia in the upper gastrointestinal tract has been claimed to occur with higher frequency in patients with renal failure, diabetes, aortic stenosis, cirrhosis, and pulmonary disease8. Previous reports on the prevalence of angiodysplasia in renal failure patients are conflicting. However, those studies used data obtained by conventional upper gastrointestinal endoscopy22,23. Our report demonstrates that angiodysplastic lesions could be responsible for OGIB in elderly patients even when not associated with other medical risk factors.

### Table 3. Binary logistic regression analysis for factors associated with angiodysplastic lesion

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>$p$</th>
</tr>
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<tbody>
<tr>
<td>Age $\geq 65$ years</td>
<td>2.76</td>
<td>1.20–6.35</td>
<td>0.02</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>1.07</td>
<td>0.31–3.73</td>
<td>0.91</td>
</tr>
<tr>
<td>Past medical history of heart disease</td>
<td>0.83</td>
<td>0.20–3.48</td>
<td>0.80</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.64</td>
<td>0.15–2.78</td>
<td>0.55</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>2.38</td>
<td>0.20–28.06</td>
<td>0.49</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>2.47</td>
<td>0.70–8.71</td>
<td>0.16</td>
</tr>
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$OR = $ odds ratio; $CI = $ confidence interval.
Our study has one major limitation due to the relatively small number of patients included and the use of a retrospective database, which, even though, was correctly built. Thus, further large prospective studies are needed to confirm our results. Moreover, given the inherently subjective nature of endoscopic interpretations, some degree of interobserver variability may have occurred in the identification of angiodysplastic lesions.

CE is a new technology developed to investigate gastrointestinal bleeding of the small intestine. It has been shown to be superior to current modalities such as small bowel barium radiology and push enteroscopy\(^{24}\). CE as a novel endoscopic procedure for small bowel diagnosis has prompted a reclassification of the terminology of gastrointestinal tract\(^{25,26}\).

The main disadvantages of CE include capsule retention\(^{27,28}\), false-negative results, and the lack of means for tissue proof or therapeutic intervention. Before using CE in patients at higher risk for capsule retention (e.g., those with Crohn disease and small bowel obstruction), patients should be made fully aware of the potential need for surgery. If patients are unwilling or unfit to have surgery, CE should not be performed. Retention of the capsule may establish a definitive diagnosis and indicate the presence of a lesion requiring surgery without precipitating acute obstruction. This was the case in one of our subjects; capsule retention was noted owing to small bowel diverticulosis, but gastrointestinal stromal tumor was found during push enteroscopy and was confirmed by surgery.

A recent meta-analysis of 24 studies included 530 patients, 310 of whom had OGIB\(^{29}\). The patients had undergone an average of 6.77 diagnostic procedures without findings. Of 727 pathologies in bleeding studies, the 317 (43.6%) that were identified by CE were vascular lesions. Our results (angiodysplastic lesions in elderly versus in total patients, 25/48 [52%] vs. 43/121 [36%]) were consistent with the results of previous studies\(^{29}\).

In conclusion, a diagnostic CE will direct appropriate medical, endoscopic or surgical interventions. The use of CE can be considered another useful tool for the physician in the evaluation of OGIB among the elderly.

References


