Aim of the study: To evaluate computed tomography (CT) findings of gastrointestinal graft-versus-host disease (GI-GVHD) occurring in children after haematopoietic stem-cell transplantation (HSCT).

Material and methods: From February 2013 to May 2018, 225 paediatric patients underwent HSCT. Sixty-eight patients (30%) presented with clinical diagnosis of acute GI-GVHD in the first 100 days after HSCT. Thirty-five (18 girls, 17 boys; age range, 2–18 years; mean age, 10.3 years) of 68 patients had abdominopelvic CT and included in study.

Results: Intestinal CT abnormalities were present in 33 (94%) and extra-intestinal CT findings were in 30 (86%) patients. Thickening of the bowel wall was the most common finding (31 patients, 89%), which involved the small bowel in 29 patients (83%), colon in 16 patients (46%), and both in 15 patients (43%). Oesophageal wall thickening was present in three patients (9%), and gastric wall thickening was in eight patients (23%). Bowel dilation was detected in 13 patients (37%). Mucosal enhancement of the bowel wall was observed in 28 patients (80%). The prevalence of the extra-intestinal CT findings were: periportal oedema in nine (26%), ascites in 15 (43%), wall thickening and enhancement of gall bladder in 13 (37%), pericholecystic fluid in six (17%), hepatomegaly in 13 (37%), and splenomegaly in nine (26%) patients. One patient (3%) demonstrated free intraperitoneal air due to intestinal perforation.

Conclusions: CT is useful to support the clinical diagnosis of acute GVHD in children with GI symptoms after HSCT. Radiological evaluation is important because early diagnosis and treatment affect the prognosis of GI-GVHD.

Key words: computed tomography, gastrointestinal system, graft-versus-host disease, haematopoietic stem cell transplantation.
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was the most common finding emerging in 31 patients (89%). Wall thickening of the small bowel (Fig. 1B, 2A–B) was seen in 29 patients (83%) whereas involvement of the colon (Fig. 1A, 3B) was observed in 16 patients (46%). Wall thickening of both small bowel and colon was more frequent (15 patients, 43%) than the isolated involvement of the small bowel (13 patients, 37%) and colon (two patients, 6%). While segmental involvement was more frequently seen in the small bowel, diffuse involvement was observed more often in the colon. Bowel dilatation was present in 13 patients (37%). Small bowel dilatation was present in nine patients (26%), and colonic dilatation (Fig. 1A) was observed in 10 patients (29%). Six patients (17%) had dilatation of the both small bowel and colon. Oesophageal wall thickening was seen in three patients (9%), and gastric wall thickening was present in eight patients (23%). Bowel mucosal enhancement was identified in 28 patients (80%). Enhancement of the colon wall (Fig. 1A) was detected in 26 patients (74%), and small bowel mucosal enhancement (Fig. 1B) was present in 20 patients (57%). Prevalence of the extra-intestinal CT findings were: periportal oedema (Fig. 2A–B) in nine (26%), ascites (Fig. 3C) in 15 (43%), wall thickening and enhancement of gall bladder in 13 (37%), pericholecystic fluid (Fig. 3D) in six (17%), hepatomegaly in 13 (37%), and splenomegaly in nine (26%) patients. One patient (3%) demonstrated free intraperitoneal air with fluid collection (Fig. 3C) owing to intestinal perforation. One patient with GI-GVHD showed multiple splenic abscesses (Fig. 3A). Figure 4 shows the numbers and percentages of the intestinal and extra-intestinal CT findings. The mean interval between the time of HSCT and the time of CT exam was 41 days. With the mean follow-up period of 30 months (range 4–57 months), 12 patients (34%) had died from acute GI-GVHD and 23 patients (66%) were alive. In this study, different intestinal and extra-intestinal CT findings were not associated (p>0.05) with GI-GVHD-related death and patient age (Table 2).

Discussion
GVHD is the major reason of morbidity and mortality in patients with HSCT. In spite of the immunosuppressive

### Table 1. Patient characteristics

| Characteristics                      | Results |
|--------------------------------------|---------|
| Age (years)                          | 10.3 (2–18) |
| Sex (M : F)                          | 17 : 18 |
| Diagnosis                            | 35 |
| Thalassemia                          | 11 (31%) |
| Acute lymphoblastic leukaemia        | 10 (29%) |
| Acute myeloid leukaemia              | 6 (17%) |
| Hemophagocytic S                     | 2 (6%) |
| Non-Hodgkin’s lymphoma               | 1 (3%) |
| Hodgkin’s lymphoma                   |         |
| Fanconi anaemia                      |         |
| Sickle cell anaemia                  |         |
| Immune deficiency                    |         |
| Osteopetrosis                        |         |
prophylaxis, clinically significant acute GVHD develops in 15–50% of adults after HSCT [3]. In this study, acute GI-GVHD developed in 30% of the paediatric patients. Acute GVHD characteristically occurs 10–40 days after HSCT (generally < 100 days) whereas persistent or recurrent acute GVHD may appear after 100 days. The mean time between HSCT and CT exam was 41 days in this study. Skin is the first and most commonly (81%) involved organ, followed by GI tract (54%) and liver (50%). The lungs, genital tract, and joints are involved less commonly [2]. Nearly half of the patients with acute GVHD progress to chronic GVHD [7]. Chronic GVHD characteristically develops 100 days after HSCT. It is related with skin changes, hyperpigmentation, dry eyes and mouth, dysphagia, diarrhoea, hepatic fibrosis, and anorexia [2, 7]. To our knowledge, CT findings of acute GI-GVHD have been defined by several studies in adults; however, no recent series has been reported in children. In this study, intestinal CT findings were observed in

Fig. 1. A) A 10-year-old boy with thalassemia. Axial CT image performed 24 days after haematopoietic stem-cell transplantation (HSCT) shows mild wall thickening and prominent mucosal enhancement of the sigmoid colon (arrow). The patient died of graft-versus-host disease (GVHD). B) An 18-year-old girl with acute lymphoblastic leukaemia. Coronal CT image taken 59 days after HSCT demonstrates marked thickening and slight mucosal enhancement of the terminal ileum (arrow)

Fig. 2. A–B) A 16-year-old girl with acute lymphoblastic leukaemia. Coronal CT images performed 38 days after haematopoietic stem-cell transplantation reveal periportal oedema (upper arrows) and moderate wall thickening of the small bowel (lower arrows). The patient died of GVHD
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Intraperitoneal free air ($n = 1$)
Pericholecystic fluid ($n = 6$)
Periportal oedema ($n = 9$)
Splenomegaly ($n = 9$)
Hepatomegaly ($n = 13$)
Gall bladder wall thickening/enhancement ($n = 13$)
Ascites ($n = 15$)
Small bowel + colon ($n = 6$)
Colon ($n = 10$)
Small bowel ($n = 9$)
Distal oesophagus ($n = 3$)
Stomach ($n = 8$)
Small bowel + colon ($n = 15$)
Colon ($n = 16$)
Small bowel ($n = 29$)

Fig. 3. A–B) A 14-year-old boy with acute myeloid leukaemia. A) Axial CT image taken 76 days after haematopoietic stem-cell transplantation shows multiple splenic abscesses (arrow). B) Axial CT image demonstrates moderate mucosal enhancement of the sigmoid colon (arrow). The patient died of GVHD. C–D) A 17-year-old girl with thalassemia. C) Axial CT image performed 47 days after haematopoietic stem-cell transplantation reveals free intraperitoneal air and fluid collection (arrow) due to intestinal perforation. D) Axial CT image shows wall thickening and enhancement of gall bladder with pericholecystic fluid (arrow). The patient died of GVHD.

Fig. 4. Intestinal and extra-intestinal computed tomography findings (%) in patients with clinical diagnosis of acute gastrointestinal graft-versus-host disease (GI-GVHD).
94% and extra-intestinal CT abnormalities were detected in 86% of the patients with acute GI-GVHD, which is similar to the ratios of 95% and 83%, respectively, reported by Shimoni et al. [1]. In this study the prevalence of bowel wall thickening was 89%, which was the most common CT abnormality and was detected more frequently in the small bowel than in the colon. These results were consistent with previous reports [1, 3, 8], which described bowel wall thickening as a significant finding of acute GI-GVHD. The frequency of bowel dilatation was 37% in this study, which was compatible with some reports [1, 3]. However, Donnelly and Morris [6] found bowel dilatation in 94% of their paediatric patients, which was significantly higher than the rate seen in this study. They suggested that multiple fluid-filled dilated bowel loops were a characteristic CT finding in children with acute GI-GVHD. Also, Brodoefel et al. [8] reported the incidence of bowel dilatation as 94% in adults with GI-GVHD. In this study, the prevalence of bowel mucosal enhancement (80%) showed similar rates with the authors [6, 8] who reported significantly higher rates of bowel dilatation. However, Shimoni et al. [1] and Kalantari et al. [3] reported lower rates of a mucosal enhancement: 16% and as 54%, respectively. The prevalence of oesophageal wall thickening was 9% and gastric wall thickening as 54%, respectively. The prevalence of oesophageal wall thickening was 9% and gastric wall thickening 16% and as 54%, respectively. The prevalence of bowel dilatation was 37% in this study, which was significantly higher than the rate seen in this study. They suggested that multiple fluid-filled dilated bowel loops were a characteristic CT finding in children with acute GI-GVHD. Also, Brodoefel et al. [8] reported the incidence of bowel dilatation as 94% in adults with GI-GVHD. In this study, the prevalence of bowel mucosal enhancement (80%) showed similar rates with the authors [6, 8] who reported significantly higher rates of bowel dilatation. However, Shimoni et al. [1] and Kalantari et al. [3] reported lower rates of a mucosal enhancement: 16% and as 54%, respectively. The prevalence of oesophageal wall thickening was 9% and gastric wall thickening was 23% in this study, which was close to the rates of previous reports [1, 3].

It should be considered that intestinal CT findings of GI-GVHD may also be demonstrated by neutropenic colitis (typhlitis), pseudomembranous colitis, drug or radiation related mucositis, and viral or fungal enterocolitis [9]. Differentiation of GI-GVHD from infectious enterocolitis is essential because GI-GVHD requires immunosuppressive treatment, which is contraindicated in infectious enterocolitis [3]. Neutropenic colitis (typhlitis) mainly involves the cecum, ascending colon, and sometimes the ileum, in contrast to GVHD. It characteristically shows caecal wall thickening with inflammatory stranding on CT [9, 10]. GI-GVHD usually involves both the small bowel and colon, but the small bowel is more often involved [2], as seen in this study. Pseudomembranous colitis is related with broad-spectrum antibiotic therapy, which affects the intestinal flora and results in overgrowth of Clostridium difficile [9]. It usually manifests as pancolitis with marked wall thickening; small bowel involvement is uncommon [2]. Drug- or radiation-induced mucositis is known as mucosal barrier injury and leads to segmental or diffuse gastrointestinal tract involvement [9]. CMV colitis shows similar findings with typhlitis [9]. Intestinal wall thickening is typically moderate in acute GI-GVHD, whereas it is usually more severe in most cases of infectious enterocolitis. Bowel dilatation and abnormal mucosal enhancement are significantly more common in acute GI-GVHD than the different infectious enterocolitis [11]. Despite these imaging findings, clinical history, time and type of HSCT, laboratory values, and stool studies are crucial for a definitive diagnosis [2].

Regarding the extra-intestinal findings, ascites was the most common finding (43%) in this study. Calantari et al. [3] found engorgement of the vasa recta (91%) and stranding of mesenteric fat (73%) as the most common extra-intestinal findings, which were not included in this study. They reported the prevalence of other extra-intestinal findings with similar rates to those seen in this study. Brodoefel et al. [8] found the incidence of biliary abnormalities to be 74%, which was the most common extra-intestinal finding in their study. Donnally and Morris [6] reported a significantly high prevalence of gallbladder-biliary abnormalities in children and suggested acalculous cholecystitis as a life-threatening complication after HSCT. Ketelsen et al. [12] revealed that cholestasis and biliary sludge were

| Computed tomography findings | Alive, n (%) | Ex, n (%) | p | n | Age | p |
|-----------------------------|--------------|-----------|---|---|-----|---|
| Small bowel                 | –            | 5 (21.7)  | 1 (8.3) | 0.294 | 6 | 11.67 ± 4.41 | 0.451 |
|                             | +            | 18 (78.3) | 11 (91.7) | 9.93 ± 5.18 | 0.594 |
| Colon                       | –            | 13 (56.5) | 5 (41.7) | 0.404 | 18 | 9.78 ± 5.10 | 0.054 |
|                             | +            | 10 (43.5) | 7 (58.3) | 17.01 ± 5.04 | 0.231 | 32 | 10.41 ± 4.88 | 0.504 |
| Distal oesophagus           | –            | 22 (95.7) | 10 (83.3) | 8.33 ± 7.506 | 0.295 | 27 | 10.19 ± 5.47 | 0.927 |
|                             | +            | 1 (4.3)   | 2 (16.7) | 3 | 8.33 ± 7.506 | 10.38 ± 3.50 | 0.927 |
| Stomach                     | –            | 19 (82.6) | 8 (66.7) | 0.125 | 26 | 10.54 ± 5.52 | 0.544 |
|                             | +            | 4 (17.4)  | 4 (33.3) | 9 | 9.33 ± 6.56 | 0.075 |
| Periportal oedema           | –            | 19 (82.6) | 7 (58.3) | 0.735 | 22 | 8.86 ± 4.76 | 0.970 |
|                             | +            | 4 (17.4)  | 5 (41.7) | 13 | 10.42 ± 4.81 | 10.27 ± 5.38 | 0.129 |
| Gall bladder                | –            | 14 (60.9) | 8 (66.7) | 0.918 | 20 | 10.82 ± 4.92 | 0.308 |
|                             | +            | 9 (39.1)  | 4 (33.3) | 9 | 9.33 ± 6.56 | 10.00 ± 4.97 | 0.927 |
| Ascites                     | –            | 13 (56.5) | 7 (58.3) | 0.275 | 22 | 11.23 ± 5.11 | 0.087 |
|                             | +            | 10 (43.5) | 5 (41.7) | 13 | 8.54 ± 4.61 | 10.31 ± 5.16 | 0.308 |
| Hepatomegaly                | –            | 13 (56.5) | 9 (75)   | 0.125 | 26 | 10.31 ± 5.16 | 0.308 |
|                             | +            | 10 (43.5) | 3 (25)   | 9 | 10.00 ± 4.97 | 10.00 ± 4.97 | 0.308 |
| Splenomegaly                | –            | 14 (60.9) | 12 (100) | 0.065 | 26 | 10.31 ± 5.16 | 0.308 |
|                             | +            | 9 (39.1)  | 0 (0)    | 9 | 10.00 ± 4.97 | 10.00 ± 4.97 | 0.308 |
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common findings and may manifest with temporary dilatation of the common bile duct.

This study had several limitations. It was a non-randomised retrospective study, it included a small number of patients, and depended on CT findings. Although all patients had a clinical diagnosis of GI-GVHD, it was not possible to compare their GI findings with a control group of other aetiologies. Biopsy was not performed in any of the patients because it was often contraindicated. Larger prospective studies may be needed to confirm the CT findings.

Conclusions

CT is useful to support the clinical diagnosis of acute GVHD in patients with GI symptoms after HSCT. Radiological evaluation is crucial because early diagnosis and treatment affect the prognosis of GI-GVHD.

The author declares no conflict of interest.

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Address for correspondence
Taner Arpaci
Department of Radiology
Acibadem Adana Hospital, Acibadem University
Cumhuriyet Caddesi No. 66,
01130, Seyhan, Adana, Turkey
e-mail: tanerarpaci@acibadem.edu.tr
Submitted: 24.08.2018
Accepted: 16.09.2018