development of endothelial damage only in a subset of patients. However, because VOD is a rather rare disease, to confirm our results it is necessary to enrol many more patients in a multicenter study.

REFERENCES


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Age and Total-Body Irradiation in Addition to Corticosteroid Dose Are Important Risk Factors for Avascular Necrosis of the Bone

This report by McAvoy et al. [1] highlights important aspects of the risk factors for the development of avascular necrosis (AVN) of the bone after hematopoietic cell transplantation (HCT). They show a clear relationship between steroid exposure and impact of steroid dose on the risk of developing AVN. Our group has recently presented data of a retrospective case-control study [2] and found some important differences compared to McAvoy’s findings. We analyzed a variety of known risk factors in a cohort of patients (cases, 50; controls, 156) without a pretransplant diagnosis of AVN undergoing allogeneic HCT (allo-HCT) from a human leukocyte antigen (HLA)-identical related donor (n = 133) or HLA-matched unrelated donor (n = 65) or umbilical cord HCT (n = 6) after either ablative (n = 142) or reduced-intensity (n = 64) preparative regimens. Median time from transplant to AVN diagnosis was 1.2 years (range: 0.12-5.2). Median follow-up was 3.7 years (range: 0.2-8.6) for AVN patients versus 1.9 years (range: 0.3-9.0) for controls (P < .001). Patients with AVN were significantly younger than controls at time of transplant (median age 37 versus 48 years, P < .001) and were more likely to have a history of tobacco use (68% versus 43%, P = .012). In univariate analyses, unrelated donor (48% of AVN patients versus 30% of controls, P = .043), use of total-body irradiation (TBI) (irrespective of dose) in preparative regimens (72% versus 46%, P = .001), and systemic steroids (SS) to treat graft-versus-host disease (GVHD) (98% versus 84%, P = .009) were associated with increased risk of AVN. Mean peak dose of SS was higher in the AVN patients versus controls (1.6 versus 1.4 mg/kg/day prednisone equivalent, P = .014). The median duration of SS treatment prior to AVN diagnosis was 228 days (range: 104-400), and 60% of these patients were receiving SS at the time of AVN diagnosis. Median total duration of SS therapy in patients with AVN was 712 days (range: 293-1195) and was significantly longer compared with the control cohort (383 days; range: 38-630) (P < .001). Interestingly, this association was seen only in patients age >40 years (AVN versus control; 852 days [range: 591-1616] versus 416 days [range: 15-596], P < .001). The finding of steroid exposure and dose relationship (function of dose and duration) was similar to what was seen in the McAvoy study, although duration of steroid use was not specifically addressed. There were no significant differences in ethnicity, gender, diagnosis, disease status, body mass index (BMI), bone density, incidence or severity of GVHD, or survival between the AVN and control patients. In multivariate analyses, age (<40 years; odds ratio [OR] = 2.55, P = .008), TBI (OR = 2.29, P = .027), and SS (1 mg/kg/day; OR = 3.48, P = 0.052) were independent predictors of AVN.

Our study identifies the use of TBI in preparative regimens as a risk factor for development of AVN. This factor was not identified in the McAvoy study, but has been previously reported [3]. In our study, age <40 years was associated with a higher risk of AVN, and is an important observation and differs from previous study, where older age has been associated with AVN [4]. The McAvoy study was controlled for age between cases and controls and thus could not address this. Pretransplant smoking was identified as a significant factor in univariate analyses and has
been reported as an association with AVN previously in a nontransplant population without steroid use [5].

Our study confirms the impact of steroid use, including duration of steroid as a risk factor for AVN after allo-HCT, and further identifies younger age and use of TBI in preparative regimens as important associations. The finding of a high rate of AVN in long-term young survivors after allo-HCT who are mostly cured of their underlying disease and have few comorbidities is of concern. The mechanism by which age influences the incidence of AVN after allo-HCT remains unknown and may involve hormonal status, bone physiology, or yet unidentified genetic susceptibilities. Our data and the report from McAvoy et al. emphasize the need for early therapeutic interventions to prevent disabling long-term complications and close follow-up in high-risk populations for AVN in an effort to improve quality of life.

REFERENCES


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