

were not selected for cardiovascular disease and a group of healthy females. Ascending and descending aorta diameters were measured by MRI at the right pulmonary artery. Average diameters were identical in both groups; however results needed to take into account a mean 20 cm difference in height between both groups. When normalized to body surface area (aortic size index) the ascending aortic diameters were significantly greater in the TS group, and close to 32% of the TS women had values >95th percentile of 2.0 cm/m². Ascending/descending aorta diameters ratios were significantly greater in the TS group. During 3 years of follow-up aortic dissection occurred in 3 women with TS. Their ascending aortic diameters ranged from 3.7 to 4.8 cm and the aortic size indices were >2.5 cm/m². This rate is almost 100 fold higher than that of normal women who are usually affected at a much later age. Unfortunately there are no prospective data to know whether dilatation of the ascending aorta preceded dissection or elongation of the transverse aortic arch—a feature more recently described in TS.

The risk for aortic dissection is greatly increased in young women with TS. Because of their small stature, ascending aorta diameters of >5 cm may represent significant dilatation. The use of an aortic size index is therefore recommended. Individuals with a dilated ascending aorta defined as aortic size index >2.0 cm/m² require close cardiovascular surveillance, and values >2.5 cm/m² indicate a high risk for aortic dissection. The authors suggested that haploinsufficiency for a pseudoautosomal gene is responsible for the linked cardiovascular and lymphatic defects in TS. In addition, it is acknowledged that this study did not provide evidence-based recommendations for the follow-up of these patients

with aortic dilatation. Further studies are also needed, like those in Marfan syndrome, to determine whether beta-blocker or rennin-angiotensin system blockade may prevent or retard aortic dilatation and if prophylactic surgery is appropriate.

Matura LA, Ho VB, Rosing DR, Bondy CA. Aortic dilatation and dissection in Turner syndrome. *Circulation*. 2007;116:1663-70.

Editor's Comment: *Recently published clinical guidelines¹ for care of girls and women with TS recommended that magnetic resonance angiography be used, in addition to echocardiography to evaluate the cardiovascular system. It was suggested that patients with defined defects be cautioned in regard to pregnancy. The present study of Matura et al provided an interesting addition of a new tool with appropriate reference data, which should help to evaluate the vital risk of aortic dissection in TS. However, prospective studies are needed which should include adolescent girls as well. The handling of the infertility issues is critical. The patients with spontaneous puberty and apparent ovarian activity should be evaluated for additional risk factors, such as systemic hypertension. The large group of infertile TS patients who have been told that assisted pregnancy can be considered in adulthood should keep in mind there is a risk of fatal aortic dissection during pregnancy. The aortic diameter should be monitored and be part of the follow-up and be taken into account in the reproductive life during adulthood.*

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The Late Effects on Childhood Cancer Survivors

Modern therapies and supportive care have increased the number of the childhood cancer survivors (CCS); as well, there has also been an increase in the late effects such as endocrine impairments and neuropsychological problems. These late effects often do not become clinically apparent until decades after cancer therapy. Unfortunately, over time the likelihood of medical follow-up decreases. Therefore, it is important for physicians to be aware of the late effects facing this population over their lifetime and the need to recall CCS patients for follow-up. However, where and by whom the follow-up of CCS can best be done is still a question that remains to be answered. Dickerman has set forth the recommendations for monitoring the late effects of CCS. He listed in a table both radiation-therapy site and chemotherapeutic agents along with the late effects that result from their use. These include: hypopituitarism, growth problems, hypogonadism, neurocognitive

defects, coronary artery disease, cardiomyopathy, lung fibrosis, interstitial pneumonitis, breast cancer, nephropathy, muscle atrophy, osteoporosis, and second cancers. He recommended that in addition to being followed by a primary care physician, all CCS patients should also attend a specialized late-effects clinic on a yearly basis. At that specialized clinic, CCS patients would be evaluated by a member of the oncology team and subspecialists such as an endocrinologist, psychologist and neurologist. Ideally, such clinics should be located in the same center in which the patient was initially treated and be available on or near the site of residence.

Dickerman JD. The late effects of childhood cancer therapy. *Pediatrics*. 2007;119:554-68.

Editor's Comment: *This is a very special review article which provides important information for*

physicians who care for CCS patients. The survival rate of childhood cancer patients has markedly improved, thus the long-term late effects, such as endocrine impairments and neuropsychological problems, have become increasingly important. These alterations may result many years after conclusion of the cancer treatment. Currently, 10 million individuals in the US are living with a cancer diagnosis, 3 times the number of survivors in decades past. In the near future 1 of 450 individuals in the population will be a long-term CCS. The 5-year survival rate of children with cancer is 80% to 85%; presently 1 in 640 individuals between 20 and 39 years of age is a CCS. Approximately 270,000 in the US present long-term morbidity of CCS.

In another paper, Oeffinger et al¹ recently reported the chronic health conditions (late effects) in adults following the treatment of childhood cancer. Their retrospective cohort study tracked the health status of adults who received a diagnosis of childhood cancer between 1970 and 1986 and compared the results with those of siblings of the patients. They calculated the frequencies of chronic conditions in 10,397 survivors and 3034 siblings (mean ages 26.6 years and 29.2 years, respectively, at the time of the study). In 62.3% of the cancer survivors there was at least one chronic condition; 27.5% had a severe or life-threatening condition. The adjusted relative risk of a chronic condition in a survivor, as compared with siblings, was 3.3 (95% CI, 3.0 to 3.5); for a severe or life-threatening condition, the risk was 8.2 (95% CI, 6.9 to 9.7). Among survivors, the cumulative incidence of a chronic health condition reached 73.4% (95% CI, 69.0 to 77.9) 30 years after the cancer diagnosis, with a cumulative incidence of 42.4% (95% CI, 33.7 to 51.2) for severe, disabling, or life-threatening conditions or death due to a chronic condition (Table). Thus, CCS have a high rate of illness owing to chronic health conditions that occurred long after the cancer was treated. There are many long-term CCS who were treated in the last 50 years, and these patients still need monitoring.

The late effects resulting from current treatment will likely decrease with improved radiotherapy being delivered with newer equipment in better fractionation schedules, along with the replacement of, or the use of, reduced doses of second-cancer-inducing chemotherapy. However, new cancer therapies used now or in the future will, in all likelihood, be associated with their own late effects. The patients who are treated with these new therapies must also be monitored closely to assess the magnitude of any late effects. It is necessary for physicians, as well as patients and family

Relative risk of selected severe (grade 3) or life-threatening or disabling (grade 4) health conditions among cancer survivors, as compared with siblings.

Condition	Survivors	Siblings	Relative Risk (95% CI)
	(N=10,397)	(N=3034)	
	percent		
Major joint replacement*	1.61	0.03	54.0 (7.6–386.3)
Congestive heart failure	1.24	0.10	15.1 (4.8–47.9)
Second malignant neoplasms†	2.38	0.33	14.8 (7.2–30.4)
Cognitive dysfunction, severe	0.65	0.10	10.5 (2.6–43.0)
Coronary artery disease	1.11	0.20	10.4 (4.1–25.9)
Cerebrovascular accident	1.56	0.20	9.3 (4.1–21.2)
Renal failure or dialysis	0.52	0.07	8.9 (2.2–36.6)
Hearing loss not corrected by aid	1.96	0.36	6.3 (3.3–11.8)
Legally blind or loss of an eye	2.92	0.69	5.8 (3.5–9.5)
Ovarian failure‡	2.79	0.99	3.5 (2.7–5.2)

* For survivors, major joint replacement was not included if it was part of cancer therapy.

† For both groups, this category excludes basal-cell and squamous-cell carcinoma (grade 2). For siblings, this category includes a first cancer.

‡ Values are for women only.

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members, to know that late effects of a cancer survivor can occur even after many years following cancer treatment. The signs and symptoms of late effects of CCS are often nonspecific and may be masked by the sequela of chemotherapy, radiation therapy, and/or surgery, and may not be clinically evident until much later in life. Therefore, they are likely to be overlooked if late effects are not actively searched for through regular follow-up. In previous issues of GGH there were 4 reviews of papers dealing with the long-term complications of CCS addressing height,² premature menopause,³ growth hormone therapy and secondary neoplasms,⁴ growth hormone deficiency, quality of life and neuropsychological function.⁵ A clinic based model for survivors of childhood cancer has been proposed by Hinkle et al.⁶

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