

interactions of other factors, such as the age and pubertal status at repair, the impact of co-morbidities, and the interaction with the extent of the defect. However, it is encouraging to note that there is an increasing acceptance by the medical community of the value of operative repair of PEx, which has long been appreciated by the surgeons who care for this patient population.

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Reference

- [1] O'Keefe J, Byrne R, Montgomery M, et al. Longer term effects of closed repair of pectus excavatum on cardiopulmonary status. *J Pediatr Surg* 2013;48:1049-54.

Letter to the Editor: Gonadal function after childhood ovarian surgery

To the Editor,

With great interest we read the article by Zhai et al. [1] in the June 2012 issue of the *Journal of Pediatric Surgery* regarding gonadal function after childhood ovarian surgery. The authors show that unilateral oophorectomy compared to ovarian salvage does not appear to impair late gonadal function after childhood ovarian surgery. Interestingly, they observed that unilateral oophorectomy appears to result in less menstrual irregularity.

This is an interesting finding, as one would expect that gonadal function would be more negatively influenced by oophorectomy than by ovarian salvage. The fact that the authors used 'cycle irregularity' as an outcome parameter for gonadal dysfunction in subjects at a mean age of 178 months (14.8 years), IQR 147–219 months (12.3–18.3 years) may have importantly influenced the conclusions as menstrual cycle regularity may not be the most reliable marker for gonadal function. Even in females with impaired ovarian reserve menstrual cycles can be completely regular. Recently, anti-Müllerian hormone (AMH) has been shown to constitute a reliable serum marker for ovarian reserve, in both prepubertal and postpubertal girls [2–4]. It is produced by granulosa cells of small growing follicles and indirectly reflects the size of the primordial follicle pool in the ovaries. It can also be easily determined in postpubertal women, since

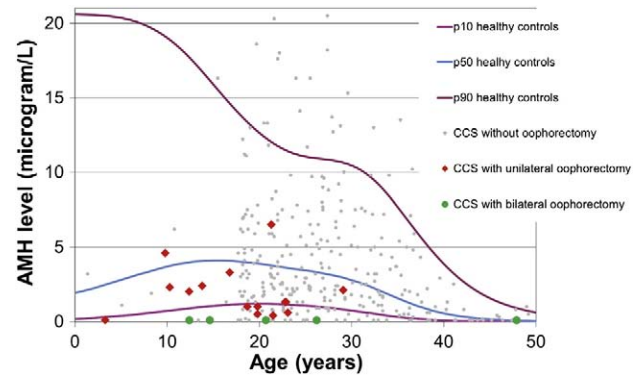


Fig. 1 Serum AMH levels according to oophorectomy in childhood cancer survivors (CCSs) in a single-center cohort. Anti-Müllerian hormone levels are compared to the p10, p50 and p90 in 250 healthy controls [2].

it is stable even during and between menstrual cycles, in contrast to FSH [5]. We recently showed in a small cohort of long-term childhood non-Hodgkin lymphoma survivors that AMH levels in survivors after unilateral oophorectomy were lower compared to AMH levels of survivors without oophorectomy, indicating an impaired ovarian reserve in NHL survivors treated with oophorectomy [6], and stressed the importance of being reluctant to remove an ovary in all children with ovarian infiltration.

In order to find support for the conclusions that oophorectomy may be performed without apparent adverse effect on gonadal function by Zhai et al, we studied serum AMH levels in a large cohort of 316 childhood cancer survivors with a median age at diagnosis of 6.2 years (IQR 2.6–11.7) and a median follow-up time of 17.3 years (11.8–23.9), and found that survivors treated with unilateral oophorectomy revealed lower AMH levels as compared to childhood cancer survivors without previous oophorectomy (Fig. 1). Survivors who were treated with bilateral oophorectomy had undetectable AMH levels. These findings suggest that ovarian reserve is reduced, even after unilateral oophorectomy, possibly resulting in premature menopause. This is in line with studies in adults showing reduced ovarian reserve after unilateral oophorectomy [7–9].

These findings illustrate that gonadal function in girls treated with unilateral oophorectomy is more compromised than was suggested by Zhai et al. This supports our earlier presented conclusion that the removal of an ovary in a child suspected of cancer should be taken with caution [7].

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References

- [1] Zhai A, Axt J, Hamilton EC, et al. Assessing gonadal function after childhood ovarian surgery. *J Pediatr Surg* 2012;47:1272-9.
- [2] Lie Fong S, Visser JA, Welt CK, et al. Serum anti-mullerian hormone levels in healthy females: a nomogram ranging from infancy to adulthood. *J Clin Endocrinol Metab* 2012;97:4650-5.
- [3] Brougham MF, Crofton PM, Johnson EJ, et al. Anti-Mullerian hormone is a marker of gonadotoxicity in pre- and postpubertal girls treated for cancer: a prospective study. *J Clin Endocrinol Metab* 2012;97:2059-67.
- [4] Visser JA, de Jong FH, Laven JS, et al. Anti-Mullerian hormone: a new marker for ovarian function. *Reproduction* 2006;131:1-9.
- [5] Hehenkamp WJ, Looman CW, Themmen AP, et al. Anti-Mullerian hormone levels in the spontaneous menstrual cycle do not show substantial fluctuation. *J Clin Endocrinol Metab* 2006;91:4057-63.
- [6] van Dorp W, Owusuua C, Laven JSE, et al. Characteristics and outcome of pediatric non-Hodgkin lymphoma patients with ovarian infiltration at presentation. *Pediatr Blood Cancer* 2013 in press.
- [7] Lass A. The fertility potential of women with a single ovary. *Hum Reprod Update* 1999;5:546-50.
- [8] Vicus D, Beiner ME, Klachook S, et al. Pure dysgerminoma of the ovary 35 years on: a single institutional experience. *Gynecol Oncol* 2010;117:23-6.
- [9] Kanat-Pektas M, Ozat M, Gungor T, et al. Fertility outcome after conservative surgery for borderline ovarian tumors: a single center experience. *Arch Gynecol Obstet* 2011;284:1253-8.

Reply to letter to the editor: Gonadal function after childhood ovarian surgery

To the Editor,

We would like to thank Dr. van Dorp and her group for their interest in our work. Their research utilizing serum AMH levels to measure ovarian reserve in childhood cancer survivors with oophorectomies is very exciting. In fact, their study in part provides biochemical evidence for our clinical conclusions. While our work showed that childhood oophorectomy did not appear to affect gonadal function, defined as fertility potential (i.e. long-term hormonal ability to achieve fecundity as measured by normal menarche and regular menstrual cycles), we also hypothesized that because "women have no compensatory mechanism for the loss of one ovary, and since the number of primordial follicles in the ovary is finite, oophorectomy may lead to a shorter reproductive lifespan" [1]. Our clinical suspicion regarding ovarian reserve was elegantly substantiated by Dr. van Dorp's study. Therefore, we continue to advocate the conservative approach to spare ovaries whenever possible. However, our study should remain reassuring in that when pathology dictates unilateral oophorectomy, the loss of a single ovary does not appear to adversely affect fertility potential, as measured by achievement of menarche and menstrual regularity.

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Reference

- [1] Zhai A, Axt J, Hamilton EC, et al. Assessing gonadal function after childhood ovarian surgery. *J Pediatr Surg* 2012;47:1272-9.