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Adnexal masses in children, adolescents and women of reproductive age in the Netherlands: A nationwide population-based cohort study

Ayke J. Hermans [a,*], Kirsten B. Kluivers [a], Laura M. Janssen [a], Albert G. Siebers [b], Marc H.W.A. Wijnen [c], Johan Bulten [b], Leon F.A.G. Massuger [a], Sjors F.P.J. Coppus [a]

[a] Department of Obstetrics & Gynaecology, Radboud University Medical Center, PO Box 9101, 6500 HB, Nijmegen, The Netherlands
[b] Department of Pathology, Radboud University Medical Center, PO Box 9101, 6500 HB, Nijmegen, The Netherlands
[c] Department of Pediatric Surgery, Princess Máxima Centre for Paediatric Oncology, PO Box 85090, 3508 AB Utrecht, The Netherlands

HIGHLIGHTS

- The incidence of adnexal masses increases quickly with age, while the risk of malignancy is highest in premenarchal children.
- The proportions of different histological subgroups vary between children, adolescents and women of reproductive age.
- Ovarian sparing procedures are related to age and are highest in adolescents and young adults.

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ABSTRACT

Objective. To provide an accurate incidence of adnexal masses in children and young women which can significantly improve the performance of current risk prediction models.

Methods. We used the PALGA database, a nationwide network and registry of histopathology and cytopathology, as the primary source of our study. Reports on ovarian histology of girls, years 1991–2014, and women aged 21–39, years 2011–2013, were included. Reports were labeled using the WHO-classification and classified as benign, borderline malignant, or malignant. Surgical procedure was scored separately.

Results. Included were 11,595 patients. The incidence of adnexal masses increased exponentially with age, from 0.43 per 100,000 womenyears at age 1 to 152 per 100,000 womenyears at age 35. A (borderline) malignancy was found in 898 (7.7%) patients, ratios between benign and malignant masses varied with age and were lowest in premenarchal children. Histology varied widely with surface epithelial tumors (35.1%), germ cell tumors (29.8%), and other cysts, tumors and tumorlike lesions (32.8%) being evenly distributed while sex cord stromal tumors were rare and only represented 2.3%. The proportion of malignancies was 6.3% in germ cell tumors while the type of malignant germ cell tumor was dependent on age. Oophorectomy was more often performed in the premenarchal age group and in women approaching the end of their reproductive age.

Conclusion. Our results show that adnexal masses in different age groups do not only differ in histological subgroups but also in malignancy rate which is of high value in presurgical risk evaluation.

1. Introduction

In children and adolescents adnexal masses are uncommon, with the incidence of neoplastic masses being estimated at 2.6 per 100,000 girls each year [1]. Several retrospective studies have been published with patient numbers varying from <20 to over 500 patients [2,3]. These populations mostly represent single centre series and present heterogenic distributions of the different histological subtypes with malignancy rates differing widely [4,5]. In women of reproductive age adnexal masses are a common phenomenon, displaying a great histologic diversity. The incidence of malignant adnexal masses in young women also increases with age [6].

Large series on the descriptive epidemiology of adnexal pathology in children, adolescents, and women of reproductive age are however lacking. The only studies available with large data sets on adnexal pathology in children and women of reproductive age are based on cancer registers such as SEER and are lacking information on benign masses [7–9].

In the Netherlands (total population 17 million) [10] the annual incidence of ovarian cancer is approximately 1300, with a mortality of 1000 women per year [11]. Considering this high mortality rate,

* Corresponding author.
E-mail address: ayke.hermans@radboudumc.nl (A.J. Hermans).

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oophorectomy may seem the best option when confronted with an adnexal mass. However fertility is a very important factor in young patients, so a thorough risk estimation should be made before surgery.

The aim of this study was to evaluate the distribution of adnexal pathology in girls (0 − 13), adolescents (14–20) and women of reproductive age (21–39) in the Netherlands over the last two decades and to provide data for use in future risk prediction models.

2. Methods

We used the PALGA registry database, a nationwide network and registry of histopathology and cytopathology, as the primary source of our study. This registry covers all hospitals in the Netherlands and contains abstracts of every histopathological and cytopathological diagnosis made from 1990 onward [12].

The search was conducted over two different time periods for two different age groups. The first search included all girls and female adolescents under the age of 21 with a report on ovarian pathology from January 1991 to July 2014. The largest time period possible was used to include all diagnoses in this unique cohort with a low incidence of adnexal masses. This search provided 7933 excerpts from 6177 patients. For the second search we identified all female patients of reproductive age (21–39 years) with a report on ovarian pathology between January 2011 and December 2013. This time period was selected to match the first search results in count to achieve a feasible number of reports to analyze, as all reports had to be individually classified according to the World Health Organization (WHO) classification of ovarian tumors by the reviewers since predefined diagnoses were not fully implemented in all time periods. The second search provided 10,298 excerpts from 8745 patients. More recent years were selected to limit the amount of reports with missing data. Patients without an adnexal mass were excluded.

Age, diagnosis, malignancy, side, surgical procedure, and the presence of torsion were extracted from each excerpt. Reports with missing data on surgical procedure were included in the tables and excluded from analysis of surgical procedure. Surgical procedures were divided in ovarian sparing and non-ovarian sparing procedures, since oophorectomy could have serious consequences for the future of children, adolescents and women of reproductive age. Ovarian-sparing procedures in benign masses were compared to ovarian-sparing procedures in malignant masses to compare the efficacy of the implementation of ovarian sparing surgery. In the absence of evidence classifying the cyst otherwise, benign simple cysts were classified as benign serous cysts. In neonates, however, benign cysts were classified as functional cysts, since most neonatal ovarian cysts are functional due to maternal estrogen, placental HCG, and fetal gonadotropins [13].

The reports were linked to a diagnosis according to the WHO classification of ovarian tumors and classified as being benign, borderline or malignant [14]. Reports were divided in four main categories: surface epithelial-stromal tumors, sex cord-stromal tumors, germ cell tumors, and other (i.e. other cysts, tumors and tumor-like lesions). Borderline malignancies were classified as malignant, when using a division in benign and malignant pathology. Masses were classified as unknown benign or unknown malignant if necroses due to torsion or chemotherapy prevented further classification of the mass. Reports with an inconclusive WHO classification were reviewed by a pathologist specialized in gynecologic pathology and classified according his conclusion.

Premenarchal status was assumed in all patients under 13, since this is the mean age of the first menstruation in the Netherlands [15].

Data were collected by the AJH and LMJ. Database consistency was checked by drafting frequency and cross-tables; inconsistent records were rechecked in the original database.

Data were analyzed using IBM SPSS version 22.0 statistical software. Descriptive statistics were used to calculate the age-specific proportion of the various histologic subtypes of adnexal masses. Furthermore, the age distribution of girls and young women 0–21 in 1990–2014 and 21–40 years of age in 2011–2013 was extracted from CBS Statistics Netherlands in order to estimate the age-specific incidence rates of adnexal masses [16,17]. Categorical data were analyzed using chi-square tests and one sample binomial tests where appropriate. Reported p-values are two-sided and results were considered significant if $p < 0.05$. Microsoft Excel 2007 was used to design the figures. The simple moving average over three years was used to design trend graphs displaying the incidence, proportion of (borderline) malignancies, the proportion of various histologic subtypes, malignancies in germ cell tumors, and surgical procedures related to age. The simple moving average over five years was used to display surgeries in patients with a benign mass. Data on percentages over a total < 5 were not included in analysis due to their limited value. Cubic splines were used to optimize the visual appearance of all graphs.

The study protocol was approved by the scientific counsel and the privacy commission of PALGA. Because only anonymized data were used, no further ethical approval was required for this study.

3. Results

The searches provided 18,231 excerpts, representing 14,922 patients. Patients without adnexal pathology ($n = 939$), with other adnexal pathology than an adnexal mass ($n = 1210$), without diagnosis ($n = 158$) or with diagnoses based on cytology only ($n = 1001$) were excluded. Revisions from patients living abroad ($n = 19$) were also excluded. Included were 11,595 patients.

3.1. Incidence

The incidence of adnexal masses increased exponentially with age (Fig. 1). The majority of the adnexal masses in children and women of reproductive age were benign, but malignancy occurred at any age. Incidence rates of adnexal masses varied between 0.43 per 100,000 women per year at age 1 and 152 per 100,000 women per year at age 35.

Incidence rates in premenarchal girls were very low. Benign cysts in girls less than a year old had an incidence of 5.70 per 100,000 girls per year, which dropped steeply after the first year. The incidence of benign tumors increased with age, from 0.34 at age 2 to 4.38 at age 12. Borderline malignancies were very rare in premenarchal children and did occur in only five cases, which were all mucinous tumors. Malignant tumors had an incidence rate ranging from 0.04 to 0.85 per 100,000 girls (below 13 years of age) per year.

3.2. Malignancy

A (borderline) malignancy was found in 898 (7.7%) patients. The proportions of benign, borderline malignant, and malignant adnexal masses varied between different age groups. The proportion of malignancy was highest in premenarchal girls, after the age of 20 this proportion was steady around 2–4%. Borderline malignancies begin to appear in early adolescence and stay constant at 2–4% after that (Fig. 2).

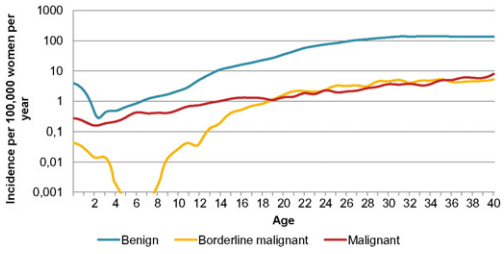

Fig. 1. Incidence rates (log scale) of adnexal masses among 11,595 women in the Netherlands, 1991–2014.