Reviewer’s report

Title: Impact of Legislation and Public Funding on Oncofertility: A Survey of Canadian, French and Moroccan Pediatric Hematologists/Oncologists

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Reviewer: Mathias Freund

Reviewer's report:

The manuscript reports on an online survey sent to 45 pediatric oncology centers in Canada, France regarding the offer of fertility preservation by ovarian tissue cryopreservation (OTC) for prepubescent girls with cancer. The survey was responded by 37% of the oncologists contacted representing 39 of the 45 centers contacted.

Ovarian tissue cryopreservation is a method for fertility preservation which has been performed in humans first time in 1999 and has been increasingly established in the last 20 years. Excellent reviews are published demonstrating the strengths and weaknesses of this method (1, 2, 3, 4). Unfortunately they are not discussed in the paper.

Furthermore a key point in the field is not adequately discussed in the paper: Differences in the establishment of ovarian tissue cryopreservation in prepubertal girls compared to girls after puberty and young women. To my knowledge only one birth after ovarian tissue cryopreservation and retransplantation has been reported worldwide in a prepubertal girl (5). There are two more reports on the induction of puberty by ovarian tissue retransplantation (6, 7).

On this background the answer of 50% of the respondents that the method is still experimental in prepubertal girls is thoroughly correct. Whether this is a reason for not discussing this possibility with the parents and their children is an ethical issue which should be in the center of the discussion of the paper. Furthermore it has to be acknowledged that proof of efficacy in a method which will restore fertility for children decades after treatment is difficult and a long-term task. So it can be questioned whether denial of reimbursement by health insurances is justified.

The presentation of results and the discussion of these questions and the topics related is poor and faulty in the paper:

Major points:

P 5, line 26
The results of our study show significant discrepancy in the provision of fertility preservation through OTC across countries. In France, almost all pediatric heme oncologist (98%) propose OTC while very few in Canada (5%) and none in Morocco (0%). (Fig 1)

There is no discrimination between counselling and discussing fertility preservation with the parents and children and recommending the method of OTC
An experimental method might be accepted or even desired by the patients but the rate most likely will not be 100% while discussing the topic and counselling should be done in a high percentage of patients. However there can even be good reasons not to do this because e.g. in acute leukemias requiring immediate treatment and leading to a substantial risk of tumor infiltration.

P 6, line 19
Cost is indeed an important reason for not offering fertility preservation. For the participants of this study, cost is one of the most important ethical issue raised by OTC

Is this really true? Was fertility preservation NOT OFFERED due to costs or not done due to costs?

P 7, line 4
In general, it appears that the offer of OTC for pediatric cancer patients is proportional to the funding by the healthcare system available in France and Quebec…

This point is related to the point on P 5, line 26. It is stated that OTC is offered to more than 90% of children in France. Acute lymphoblastic leukemia is the most common neoplasia in childhood. In many cases it can be reasonable not to recommend OTC due to medical reasons, but this decision has to be discussed with the patients/their parents. The presentation of this result raises many questions not answered in the paper.

P 7, line 60
In France and Morocco there is a paternalistic model, while in Canada there is a model based on the principle of autonomy.

Based on the deficiencies in the presentation of results these conclusions are not justified.

P 8, line 16
Promoting the offering of OTC for prepubescent girls: an ethical obligation

This is an onesided view without justification. Based on the still experimental nature of the method counselling and discussing OTC is justified and it can be offered to those patients who want it. Promotion or propagation should be ethically restricted to medically established methods.

P 8, line 24
At the same time, emerging data suggest it has the potential to become an established fertility preservation method in the near future (7, 22)

This statement is not justified on the literature cited:
Citation 7 refers to the ASCO Clinical Practice Guideline. In the publication OTC is stated as still experimental in ALL AGES but a potential is stated for the future. There is no statement on prepubertal girls.
Citation 22 refers to a publication with video on the laparascopic procedure in a 6 year old girl (8).

P 8 line 26
International recommendations from a 2016 expert meeting conclude that the best candidates for OTC are prepubescent girls (23)
This is not true. Statement in the cited publication: Although ovarian tissue cryopreservation is still an experimental strategy, it might be proposed to selected patients. In particular, this method is the only available option to preserve fertility in prepubertal girls who are candidates to gonadotoxic therapies (9).

These uncritical reflections on OTC are in a sharp contrast to the discussion done in page 10 which has obviously written by another person.

Minor points:
P 2, line 27
the only alternative for pre-pubertal girls is ovarian tissue cryopreservation
This is questioned by Mertes (10)

There are deficiencies in the terminology: "pediatric heme oncologist" is no commonly accepted term - it should be: "Pediatric hematologist/oncologist"

Reference List


8. Rovigatti U. Chronic Fatigue Syndrome (CFS) and Cancer Related Fatigue (CRF): two "fatigue"


**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
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Unable to assess

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No

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