How Do Adolescent Minors Banking Sperm Before Cancer Therapy Subsequently Use The Fertility Service? A Post Banking Re-evaluation.

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BACKGROUND

More and more adolescents are surviving cancer.
But treatments may be gonadotoxic.
Fertility is a potential reproductive right.
Minors deemed sexually mature have been offered the chance to bank sperm before treatment at University College Hospital since 1999.
We previously reported our experience in 166 adolescents offered banking at diagnosis.

OBJECTIVES

1. To re-evaluate how many patients banking sperm successfully (GpA) returned for post treatment re-evaluation compared with those who attempted but failed (GpB).

2. To compare longitudinal sperm counts, fertility rates and survival, by group and prior gonadotoxicity risk.

METHODS

Retrospective collection of post treatment survival, semen analysis (sperm count, concentration, motility and volume), and biochemical (LH/FSH/ testosterone) parameters in 76 of 117 patients who succeeded in their attempt to bank sperm between 2000-2010 and of whom 38/117 returned for re-evaluation .

GpA) Successful: any viable sperm banked (n76).
GpB) Unsuccessful: azoospermia or necrospermia (n17).
GpC) Unable: to produce a sample (n24).

Gonadotoxicity Risk
The risk of developing subfertility based on the initial treatment regimen was graded:

1) Low < 20% 2) Medium 20 – 80% 3) High > 80% as per current UK guidance.

"**Infertility**" was defined as FSH >15iu/l or azoospermia.

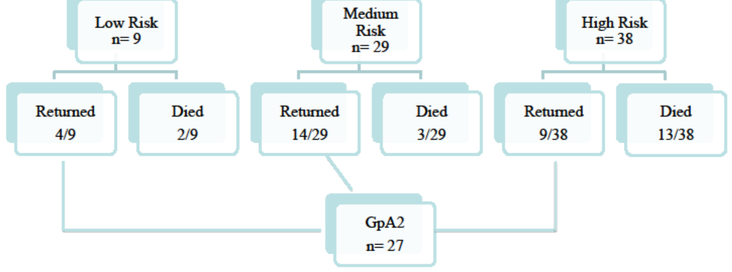
Data are shown as median and range; intergroup comparisons were made using non parametric statistics. P values < 0.05 were significant.

Table 1 – original entire cohort of those who attempted to bank initially

Group	Age (years)	Chemo	n	Died	Re-evaluated
A n76	Successful 15.11 [13.04-22.08]	Before 1st line chemo	69	17	24
		Relapsed pre 2nd line chemo	7	1	3
		Total	76	18	27
B n17	Unsuccessful 15.00 [12.09-17.09]	Before 1st line chemo	12	4	3
		Relapsed pre 2nd line chemo	5	1	2
		Total	17	5	5
C n24	Unable		24	3	5

RESULTS

fig 1 Flow diagram of Group A (Successful)



1. n76 (GpA) successfully banked sperm. n69 banked at diagnosis, n7 during 2nd remission.

2. n18 died at a median follow up of 2.10[0.01-5.30] years.

3. n27 (GpA2) attended for re-evaluation of fertility at 24.4[18.20-29.80] years of age.

4. No difference in baseline demographics (age, initial FSH, gonadotoxicity risk or semen parameters) between returning, non-returning and deceased patients: Kruskal-Wallis H test (X2 >0.05).

GpA2: Re-evaluated Successful group (n27/76)

1. 6/23 (26%) medium and high-risk patients are now potentially infertile (n2 have FSH >15iu/l and n4 sperm count < 6 million/ml)

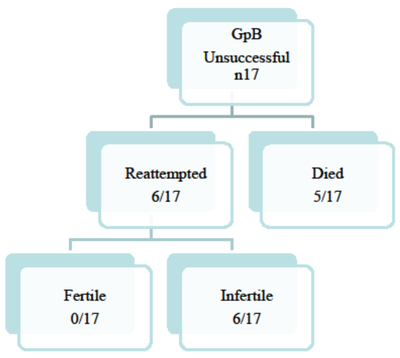
2. All 4 returning low risk patients have preserved fertility (sperm counts >6million/ml and FSH<15IU/).

4. A significant minority at highest risk 13/38 (34%) died.

5. There was no significant change in biochemistry in available paired data: FSH (n7), LH (n8), testosterone (n4) (Wilcoxon all p>0.5).

6. Paired sperm count (n6), sperm concentration (n13) and sperm motility (n12) were also unchanged (Wilcoxon p>0.05), but sperm volume (n15) increased over time (p=0.001).

fig 2 Flow diagram of Group B (Unsuccessful)



1. n17 patients aged 15.00[12.09-17.09] years (GpB) failed to bank at diagnosis (n12) or 2nd remission (n5).

2. 5/17 (29%) died at a median 1.35[0.6-2.50] years of follow up and 1.51[0.05-3.94] years after their first unsuccessful banking attempt.

1. 5/17 (29 %) reattempted, again unsuccessfully, to bank sperm aged 23.6[21.90-26.50] years. Sperm concentration, count and motility all remained poor but only 1/3 patients with available biochemistry had a predictably high FSH >15i/l.

Group C (Unable)

1. GpC were younger and failed to produce a specimen on initial assessment.

1. n5 who returned for re-evaluation had no biochemistry; 2 of these are infertile and 1 low risk ALL patient has retained fertility (sperm concentration of 6.9 million/mil, count of 28 million and motility of 57%.)

Intergroup analysis by gonadotoxicity risk

Low risk:
9/15 patients considered at low risk of gonadotoxicity banked initially; n2 died and 4 returned a median 9.75[8.80-10.20] years later, aged 25.50[24.70-26.10] years. One other unable to bank at diagnosis, returned and banked successfully. All successful bankers remain fertile with a median sperm count of 43.45[36.5-50.0] million.

Medium risk:
18/29 patients who initially banked at 16.00[13.04-22.08] years were re-evaluated 8.25[3.80-14.00] years later aged 23.80[19.80-29.80] and 4 had died. 14/18 retained fertility, but 4 are now potentially infertile (n3 sperm count of 0.1 million, FSH 16.5IU/L)

High-risk:
Of 38 patients who initially banked aged 15.10[13.05-18.01] years, 20 died aged 17.09[14.11-22.01] and 9 were revaluated 6.80[3.70-9.80] years later aged 23.60[18.20-26.50]. Of these 2/9 have potentially become infertile: n1 has FSH >15 (normal sperm count) and n1 is azoospermic.

At reassessment, sperm concentration was higher in patients receiving low gonadotoxicity risk treatment than those receiving medium (p=0.008) or high-risk (p=0.021) therapy

CONCLUSIONS

- Low gonadotoxicity risk patients at low priority for fertility preservation were correctly identified before treatment.
- High risk patients need prioritising but were least likely to survive and therefore be able to use the banked sperm.
- Patients azoospermic or necrospermic at initial attempt (GpB survivors) showed no signs of recovering fertility up to 11 years later.
- The low survivor re-evaluation rates suggest improved post treatment endocrine/fertility assessments are required to properly assess the cost benefit of fertility preservation to underage patients.

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