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Title:
MANAGEMENT OF FLUID ACCUMULATION WITHIN THE ENDOMETRIAL CAVITY DURING A FROZEN EMBRYO TRANSFER CYCLE

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Background:
Although it is not uncommon to observe fluid within the uterine cavity at the start of a synthetic preparation cycle for a frozen embryo transfer (FET), occasionally, fluid can persist up to and including the day of FET. While published data has focused primarily on the impact of structural lesions including polyps and fibroids on IVF outcomes, it remains uncertain whether the presence of fluid within the endometrial cavity influences endometrial receptivity and embryonic implantation.

Objective:
The study sought to evaluate FET cases in which patients experienced persistence of fluid within the endometrial cavity to better formulate best practice strategies for clinical care.

Materials and Methods:
Using a natural language processing approach, patients undergoing FET cycles associated with key terms such as “endometrial fluid” were identified within the center’s electronic medical record. Results were manually reviewed for accuracy. Patients were segregated into groups based on branch points describing actions taken when endometrial fluid did not spontaneously
resolve (e.g. aspiration vs. cancellation). Recurrence of endometrial fluid accumulation and pregnancy outcomes for each group were recorded (Figure 1).

**Results:**

A total of 298 cycles (between the years 2003-2017) were identified. One hundred and nineteen (39.9%) patients had fluid present on cycle day 3 at initial administration of estrace. The remaining 179 (60.1%) patients showed no evidence of fluid at initial administration of estrace, but subsequently developed endometrial fluid later in their cycle.

The majority (n=233; 78.2%) of cycles affected by endometrial fluid during the follicular phase experienced spontaneous resolution. Of these, 147 (63.1%) cycles had a positive pregnancy test, while the remaining 86 (36.9%) did not.

In cases (n=65) where endometrial fluid did not spontaneously resolve, 52 (81.5%) cycles were cancelled, and 12 (18.5%) underwent aspiration of the endometrial fluid. Of patients (n=53) whose cycles were cancelled, 18 (34%) experienced recurrence of endometrial fluid in subsequent FET cycles, 22 (41.5%) did not experience further episodes of fluid accumulation, and 13 (24.5%) did not undergo additional cycles. Of patients (n=12) undergoing aspiration of endometrial fluid, 6 (50%) had persistence or recurrence of endometrial fluid resulting in cancellation of the cycle, and the other 6 (50%) experienced resolution. Following resolution of endometrial fluid after aspiration, 1 patient (16.7%) had a positive pregnancy test, whereas 5 (83.3%) had negative tests.

**Conclusions:**

Following menses, sonographic observation of intrauterine fluid is not uncommon and does not appear to impact cycle outcome. Intra-cycle identification of transient accumulations of fluid are also common, and if spontaneous resolution occurs, the success of the cycle is unaffected. Persistent accumulations of fluid are often felt to be pathological and potentially related to uterine scarring. Of the cycles affected, the majority were cancelled by the physician and diagnostic and therapeutic interventions were introduced. Aspiration of endometrial fluid resulted in resolution in half of the cases. Unfortunately, pregnancy rates in this group remained low. Large scale data analysis and multi-center collaborative trials will ultimately help identify patterns of disease, efficacy of interventions, and prognostic variables.
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Figure 1:
Decision tree describing outcomes of cycles affected by endometrial fluid during the follicular phase of a synthetic preparation cycle for frozen embryo transfer