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Cost Analysis Model of Outpatient Management of OHSS with Paracentesis: ‘Tap Early and Often’ Versus Hospitalization

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Abstract

Objective—To compare the cost of two treatment regimens for moderate to severe ovarian hyperstimulation syndrome (OHSS); conservative inpatient versus outpatient management with paracentesis.

Study design—A decision tree mathematical model comparing conservative inpatient versus outpatient management of moderate to severe OHSS was created. The common final pathway of either management was resolution of OHSS. Sensitivity analyses were performed over the range of variables.

Main outcome measure—Total management cost of ovarian hyperstimulation syndrome.

Results—The cost of conservative therapy including first tier complications was \$10,098 (range \$9,655 to \$15,044). The cost of outpatient management with paracentesis was \$1954 (range \$788 to \$12,041). This resulted in an estimated cost savings of \$8,144 with outpatient management with paracentesis. One-way sensitivity analyses were performed. Varying the probability of admission after outpatient treatment still indicated outpatient treatment was the most cost effective (probability=1.0, cost \$6,110). Varying the duration of hospitalization with primary inpatient treatment was equal to outpatient treatment costs only at a stay of 0.71 days or shorter.

Conclusion—Our model suggests early outpatient paracentesis for moderate to severe OHSS is the most cost effective management plan when compared to traditional conservative inpatient therapy. The cost savings for outpatient management persisted throughout a variety of outcome probabilities.

Keywords

ovarian hyperstimulation syndrome; OHSS; paracentesis; cost-analysis; outpatient management; ART; cost

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Introduction

Moderate to severe ovarian hyperstimulation syndrome (OHSS) occurs in 1–5% of assisted reproductive technology cycles and carries the potential for severe complications.(1–3) OHSS is characterized by increased capillary permeability, resulting in a significant fluid shift and accumulation in the peritoneal space.(4–6) Common signs/symptoms include shortness of breath, nausea, vomiting, abdominal discomfort, and abdominal distention. The tense ascites may cause hemodynamic instability, respiratory compromise, and oliguria. Potentially lethal complications include thromboembolism, renal failure and adult respiratory distress syndrome.(7)

Traditional management of OHSS consists of hospitalization with supportive therapy: intravenous fluids, bed rest, and monitoring. Several prospective and retrospective trials have documented the course of inpatient management.(8–14) An alternative strategy of treatment for OHSS consists of early intervention with paracentesis in an outpatient setting. In 1994, Shrivastav et al.(15) reported a comparison of inpatient versus outpatient treatment of severe OHSS and concluded that outpatient management was a safe and effective treatment alternative. The authors (15) noted that patients with early paracentesis reported immediate improvement in symptoms as compared to their inpatient cohort who were “all uniformly uncomfortable.” Those treated with outpatient paracentesis also had a shorter duration of symptoms. The efficacy of outpatient treatment has been confirmed in two subsequent studies. (17–18) Lincoln et al. (18) reported that 92% of patients with moderate/severe OHSS treated with outpatient paracentesis successfully avoided hospitalization. Fluker et al. (17) reported that the only OHSS patients hospitalized during their study of outpatient management were due to non-medical reasons. All of these studies reported no adverse outcomes with the use of outpatient treatment, even when multiple paracenteses were performed.

While many practitioners agree that paracentesis can be beneficial for treatment of severe OHSS, treatment of moderate OHSS with paracentesis is less uniformly agreed upon. Nevertheless, even with primary inpatient management, paracentesis has been shown to decrease the total time of hospitalization compared to inpatient therapy alone from an average of 11 days to 4 days, respectively. (9,11)

We were unable to find studies that compared the economic consequences of outpatient paracentesis to hospitalization for moderate to severe OHSS. While conservative inpatient therapy is considered by some to be the most conservative treatment option, the resources consumed are significant and the prolonged duration of OHSS may predispose the patient to complications, such as thromboembolism. The financial burden of OHSS treatment appears to be most related to the duration of hospitalization. We therefore undertook this cost-minimization analysis to evaluate the two treatments across a wide variety of variables and determine which management option is the most cost-effective treatment.

Materials and Methods

Study Design

A decision tree model comparing conservative inpatient versus early outpatient management of moderate to severe OHSS was created. The common final pathway of either management was resolution of OHSS. Outcome probabilities and effectiveness of outpatient management with paracentesis were derived from published sources as well as internal institutional data through a retrospective chart review (see below).

Decision Tree

The analysis was performed from a cost-minimization perspective. A decision tree was created with TreePlan 1.70 (Decision Toolworks, San Francisco, CA) and is illustrated in Figure 1. The decision tree begins with a diagnosis of moderate to severe OHSS. The decision node models for selection of either conservative inpatient management or early outpatient treatment with paracentesis.

Within the conservative inpatient arm, we modeled spontaneous resolution (with supportive therapy), inpatient paracentesis, as well as potential intensive care unit (ICU) admission as possible outcomes. The early outpatient management arm consisted of four potential outcomes to include: 1) spontaneous resolution after first paracentesis, 2) the necessity to perform a repeat paracentesis, 3) admission to general gynecologic inpatient ward, and 4) admission to an ICU setting.

For our model, we determined the probability of each event node either from published data, (8–19) or from our experience with outpatient management (see below). There were eleven published manuscripts describing treatment of moderate/severe OHSS which were utilized in the design of the decision tree. A summary of the literature reviewed is shown in Table 1. Length of inpatient stay (days) and number of outpatient visits were based upon published literature. The outcome probabilities used in the decision tree (with their associated standard deviation and 95% confidence intervals) are shown in Table 2. Costs were derived from Strong Memorial Hospital, Rochester NY. This site was selected as a representative of a medium sized tertiary hospital in a medium sized city to reflect average costs. All costs were 2007 estimates (Table 2). The mathematical model was based upon general costs applied to published OHSS probability outcomes, as direct management costs have not been previously reported in the literature. The components of a typical laboratory workup of OHSS included a complete blood cell count, complete metabolic panel, liver function tests, and urinalysis. It was assumed that for either treatment arm that an initial transvaginal ultrasound would be performed to assess the amount of ascites. Within the outpatient setting, paracentesis was assumed to be vaginal culdocentesis with removal of ascitic fluid.

Retrospective Review of OHSS

To determine the probabilities and outcomes associated with early paracentesis in the outpatient setting, we conducted an institutional retrospective review of OHSS management that was approved by the Walter Reed Army Medical Center Division of Clinical Investigation (Institutional Review Board). All patients were identified by a diagnosis of moderate to severe OHSS who were treated with primary outpatient management with paracentesis from the years 2000–2007. The diagnosis of moderate or severe OHSS was based upon the classification system by Golan et al.(20) A decision for paracentesis was made when the patient demonstrated significant symptoms as a result of tense ascites. Criteria for early intervention with paracentesis included: abdominal pain, inability to tolerate oral intake, inability to lie flat, or dyspnea. In addition, paracentesis was performed if biochemical evidence of moderate/severe OHSS was present such as hematocrit >45%. The paracentesis was performed transvaginally under ultrasound guidance utilizing vacuum aspiration of all obtainable ascitic fluid through the posterior cul-de-sac. In patients with evidence of severe hemoconcentration (hematocrit >45%), prophylactic anticoagulation was initiated with subcutaneous injectable low molecular weight heparin and was typically continued for 3–4 weeks after symptom resolution. Criteria for hospitalization was: failure to respond sufficiently to tolerate oral fluids, dehydration, or requirement for supportive care, such as pain control, as determined by the managing team.

A complete review of electronic medical records was performed and outcome information was recorded to include number of outpatient visits, number of paracenteses performed, number of patients who subsequently required inpatient admission, inpatient length of stay, and pregnancy rates.

Statistical Analysis

All probabilities and treatment days/visits were expressed as mean with standard deviation and 95% confidence intervals. The decision tree was modeled for a cost-minimization strategy. One-way sensitivity analyses were performed over the range of patient costs, outcome probabilities and length of hospitalization. Two-way sensitivity analyses were performed when appropriate.

Results

Patients diagnosed with OHSS from January 2000 to December 2007 at Walter Reed Army Medical Center were included in the retrospective analysis. Twenty-nine (29) patients were identified with moderate/severe OHSS and treated with primary outpatient management with early paracentesis. The mean number of paracenteses performed was 1.76 ± 1.18 (range 1–6). There were twelve patients who required a second paracentesis (41%) and six patients who required a third paracentesis (21%). Eight patients (27.6%) were admitted for either for pain control or intravenous hydration (inability to tolerate oral fluids), a percentage somewhat higher than previously reported in the private sector, perhaps relating to the fact that military patients do not incur costs for hospitalization. The mean number of admission days was 2.0 ± 0.9 (range 1–3). These data were incorporated into the decision tree model and supplemented the published literature, as appropriate. The overall pregnancy rate for these twenty-nine patients was 79.3%.

Based upon our model, the cost of conservative therapy including first tier complications was \$10,099 (range from \$9,655 to \$15,044). The cost of outpatient management (Figure 1) with early paracentesis and its first tier complications was \$1954 (range from \$788 to \$12,041). This resulted in an estimated cost savings of \$8,144 per patient treated with early intervention with paracentesis and outpatient management compared to hospitalization.

One-way sensitivity analyses were performed in order to demonstrate the stability of the conclusions over a range of variables. While keeping the cost of outpatient management constant, varying the duration of hospitalization with primary inpatient treatment (Figure 2A) was equal to outpatient treatment costs only at a stay of 0.71 days (a nonsensical value). Varying the probability of admission after outpatient treatment (Figure 2B) did not change the conclusion that outpatient treatment was the most cost effective treatment (probability=1.0, cost \$6,110). The lower cost of outpatient management even with subsequent 100% hospitalization was an effect of the shorter duration of hospitalization (compared to primary inpatient therapy) that has been reported following outpatient paracentesis.

Further analysis revealed that even if all patients managed with outpatient treatment required three paracenteses prior to resolution, the cost of outpatient treatment increased only to \$2,851. The main improvement factor with primary outpatient management was the lower likelihood for prolonged hospitalization than the conservatively managed group. A two-way sensitivity analysis (simultaneously manipulating both the probability of outpatient management hospitalization and the duration of inpatient hospitalization) revealed again that inpatient treatment was equal in cost to outpatient management only when the length of hospitalization was less than one day.

Discussion

Outpatient treatment of moderate to severe OHSS with early paracentesis has been shown to be safe and effective. (15,17,18) Our model suggests that early intervention with outpatient paracentesis is a cost-minimizing strategy when compared to traditional conservative inpatient therapy, resulting in a savings of \$8,144 per patient treated. The cost savings for outpatient management persisted throughout a variety of outcome probabilities and treatment days.

Within the model, we compared conservative inpatient management (supportive therapy) versus early outpatient management with paracentesis and found a significant cost discrepancy. Because the average hospitalization with purely supportive therapy was considerably longer than with inpatient therapy incorporating paracentesis, it was expected this magnified the cost discordance. In order to correct for this, one-way and two-way sensitivity analyses were performed. The analysis revealed that only at a nonsensical value (inpatient stay of 0.71 days) would the cost of inpatient management equal that of outpatient treatment. This indicates that inpatient treatment, with or without paracentesis, increases the cost burden due to the longer duration of hospitalization reported in the literature (mean 7.45). However, even when the intended plan was outpatient management, we noted that roughly 13% (based on the literature) or 25% (based on our experience) of patients ultimately required admission, usually for hydration or pain control. Thus hospitalization cannot be avoided in all cases. Still, as demonstrated in Figure 2B, even at considerably higher probabilities of hospitalization such as 60% or higher, initial outpatient management remains the most cost-effective treatment strategy.

The strength of this analysis was that the conclusions remained unchanged over a wide variety of variables. The sensitivity analyses demonstrated that the study's conclusions were robust. The variables were tested beyond a range that was clinically reasonable, yet they continued to support the conclusion that outpatient paracentesis was the most cost-effective plan.

The safety of outpatient management (with paracentesis) of OHSS has been well documented. Initially, Shrivastav et al. (15) reported safety among his outpatient cohort. Later, both Fluker et al.(17) and Lincoln et al.(18) confirmed the safety and efficacy in the treatment of women with moderate to severe OHSS through the use of outpatient paracentesis and intravenous fluid hydration. Subsequent hospitalization was uncommon and no complications were noted in these patients.

The primary outcome of this analysis model was the economic difference between two accepted managements of ovarian hyperstimulation syndrome. To our knowledge, this is the first report of a cost-analysis comparison on this topic. When two different regimens have been shown to be equally safe and efficacious, the financial aspect must be considered. As stated by Van Voorhis (16), a clinician's "primary concern is the welfare of the patient... Nevertheless, economic considerations are becoming an increasingly important fact of medical practice so an understanding of cost-effective medical practice is of importance to the clinician as well." Our data support primary outpatient therapy with paracentesis as cost-minimizing throughout a series of clinical scenarios.

One remaining concern is whether symptomatic management is, in fact, equal between the two treatment approaches, conservative supportive versus early paracentesis management. Our anecdotal experience as well as the experience by Shrivastav et al.(15) support that early paracentesis results in immediate improvement in patient's symptoms. Given that symptoms are the primary indication for paracentesis, management with early paracentesis may be the more prudent choice for patient comfort.

The primary weakness of any decision tree analysis is the design which relies upon assumptions and a number of fixed outcomes. We attempted to minimize the error of assumptions by collecting data from multiple sources. Our institutional data were limited by small numbers (29 patients managed with outpatient paracentesis in 7 years). For this reason, the assumptions within our analysis are supported by published data from eleven studies over the past nineteen years in addition to our own institutional data. While some variation exists among the different trials, the results appear consistent. It should be recognized that the model was based upon costs applied to published OHSS probability outcomes, as the direct costs of OHSS management previously have not been reported in the literature. Another inherent weakness, a limited number of fixed outcomes, poses a challenge to the model. Within the literature review, there were no reported rates of complications and all reported outcomes fell within the confines of our model. It is possible that currently unquantifiable issues could alter the model and its cost-effectiveness. This model assumed that if such issues existed they were rare and would have minimal impact. Although not described in the current literature review, a legitimate concern with multiple paracenteses is the risk of infection or other serious complication (vessel injury, etc.) which may ultimately result in a more costly situation.

The ideal way to compare the safety, efficacy, and cost of these two treatments would be through a randomized controlled trial (RCT). However, when examining a relatively uncommon complication such as OHSS, a RCT poses a challenge because it requires significant resources and patient numbers to have sufficient statistical power. A reasonable way to assess the relative cost value of two competing approaches, therefore, is with the use of mathematical modeling techniques. Mathematical modeling here utilizes the best available information on OHSS treatment, but does not substitute for a prospective clinical trial.

In conclusion, our model suggests outpatient treatment of moderate to severe OHSS with early intervention using paracentesis appears to be the most cost-effective management option. Outpatient paracentesis deserves consideration as the primary treatment modality for ovarian hyperstimulation syndrome.

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Figure 1.

Cost-effective decision tree for management of OHSS. Initial arm is a decision node between inpatient or outpatient management. After deciding treatment route, all subsequent outcomes were based upon probabilities extracted from literature or institutional retrospective chart review. The final outcome for either treatment arm was resolution of OHSS. Cost estimates from 2007 were used. Costs listed in each box of the outline are the total costs per patient enrolled for that treatment arm and outcome.

Figure 2.

A. Cost variation through range of inpatient hospital stay lengths. The cost of outpatient management arm is held constant in this one-way sensitivity analysis. Axes: x = length of inpatient hospitalization in days, y= total cost of treatment (US dollars). The intersection of the lines demonstrates cost equivalence between two treatment arms which occurs at less than 1 day of hospitalization.

B. Cost of primary outpatient management of OHSS through a range of probabilities of hospital admission. Inpatient management cost is held constant in this one-way sensitivity analysis. Axes: x= probability of hospital admission in primary outpatient treatment arm, y=

total cost of treatment (US dollars). The point of intersection between the two lines would represent cost equivalence, but as shown, inpatient management remains more costly, even at high probabilities for hospitalization.

Table 1
Summary of literature on the inpatient and outpatient management of moderate/severe OHSS.

Author	Date	Method	Total OHSS	Outpatient Management with Paracetesis	Inpatient Management	ICU Admission
Borenstein	1989	Retrospective	39	0	39	0
Aboulghar	1990	Prospective	21	0	21	0
MacDougall	1992	Retrospective	15	0	15	1
Aboulghar	1993	Retrospective	52	0	52	0
Shrivastav	1994	Prospective	18	10	8	0
Fluker	2000	Prospective	14	14	0	0
Myrianthefs	2000	Retrospective	10	0	10	10
Lincoln	2002	Retrospective	48	48	0	0
Klemetti	2005	Retrospective	330	0	330	0
Papanikolaou	2005	Retrospective	113	0	113	0
Papanikolaou	2006	Prospective	53	0	53	0

Table 2

Summary of OHSS management probabilities, average hospital stay, and management costs.

Variable	Mean	SD	Range (95% CI)	
Days				
Inpatient Stay (with conservative mgmt) ^{8–11,13–5,19}	7.45	0.77	5.93	8.97
ICU Stay ^{10,19}	4.82	3.02	–1.10	10.74
Inpatient Stay (after attempted outpatient mgmt) ^{17–18}	3.69	0.62	2.49	4.89
Probabilities				
Outpatient Mgmt Admitted to Hospital ^{17–18}	0.130	0.036	0.059	0.200
Outpatient Mgmt Requiring 2 nd Paracentesis ^{15,17}	0.548	0.017	0.033	0.581
Outpatient Mgmt Requiring 3 rd Paracentesis ¹⁷	0.262	0.017	0.229	0.295
Inpatient Mgmt Requiring Paracentesis ^{8–11,13–15}	0.266	0.596	0.149	0.383
Inpatient Mgmt Transferred to ICU ¹⁰	0.067	NA ^a	NA	NA
Comprehensive Costs ^b				
Outpatient Visit with Paracentesis (per visit)	\$788			
Inpatient Hospital Stay (per day)	\$1,296			
ICU Inpatient Stay (per day)	\$3,036			
Individual Costs ^b				
Laboratory Evaluation (CBC, Hepatic Panel, Chemistry, Urinalysis)	\$216			
Intravenous Fluids	\$162			
Transvaginal Ultrasound	\$190			
Vaginal Paracentesis (Culdocentesis)	\$220			

^aData not available

^bCost estimates obtained from Strong Memorial Hospital, Rochester NY (representative of a medium sized tertiary hospital in a medium sized city to reflect average costs). All costs were 2007 estimates. ⁸⁻¹⁹References from which data was extracted. All reference numbers correspond to the respective references within the text. Csokmay et al. data included where appropriate.