Repeat Large-Volume Paracentesis Versus Tunneled Peritoneal Catheter Placement for Malignant Ascites: A Cost-Minimization Study

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OBJECTIVE. The objective of this study was to determine the point in time at which tunneled peritoneal catheter placement becomes less costly than repeat large-volume paracentesis (LVP) for patients with malignant ascites.

MATERIALS AND METHODS. Procedure costs were based on 2013 Medicare reimbursement rates. Rates for specific complications were obtained from the literature and were assigned costs. A decision tree–based Markov chain Monte Carlo model was designed with 11 cycles of 10 days, to simulate 4000 subjects per trial. Patients were grouped according to initial treatment decision (LVP vs catheter placement), and the total cost at the end of each 10-day cycle was calculated. The point at which catheter placement became less costly than LVP was determined. Additional simulations were used for bivariate analyses of all cost and probability variables and for trivariate analysis of cycle length and volume of fluid drained per cycle.

RESULTS. Individual input probabilities were not significantly different from corresponding simulation outcomes (p value range, 0.068–0.95). When complications were included in the model, the cost curves crossed at a mean (± SD) of 82.8 ± 3.6 days (range, 75.8–89.6 days), corresponding to a time between the performance of the ninth and 10th LVP procedures. Intersection occurred earlier in simulations with a shorter cycle length and less fluid per cycle, but it was minimally affected by changing individual complication probabilities and costs.

CONCLUSION. For patients with malignant ascites, LVP becomes more costly once the procedure is performed nine or 10 times or at approximately 83 days, if paracentesis is repeated every 10 days, with 5 L of fluid removed each time. Use of a tunneled peritoneal catheter improves the cost advantage for patients who receive LVP more frequently or patients who have less than 5 L of fluid drained per procedure.

Keywords: interventional radiology, malignant ascites, palliative care, paracentesis, tunneled peritoneal catheter

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It is now understood that ascites caused by malignancy has a different pathophysiologic profile than does ascites resulting from portal hypertension [1–7]. Paracentesis has been shown to be the most used (and is generally considered the most effective) treatment for patients with ascites [8]. Unlike in the management of benign ascites, the use of prophylactic antibiotics for spontaneous bacterial peritonitis occurring between paracentesis procedures is generally not indicated for patients with malignant ascites, because these patients do not have a significant risk for such infections [9]. In addition, there is no evidence for the use of concomitant plasma expanders for hypotension prophylaxis [3, 5]. In fact, complications occur very infrequently in patients with malignant ascites, although rare complications include secondary peritonitis, hypoproteinemia, pulmonary embolism, bowel perforation, and hypotension [1–5, 10–13]. The greatest drawback associated with the use of paracentesis in this patient population is the need for repeated procedures, because symptomatic relief may last only a few days; patients typically need to have a paracentesis procedure performed every 10–14 days on average [2–5, 12–15].

The National Institute for Health and Clinical Excellence recently recommended that the National Health Service of the United Kingdom adopt the use tunneled peritoneal catheter (TPC) drainage systems for ascites management, on the basis of evidence of good efficacy, low complication rates, improved quality of life, and cost savings [11, 16]. To our knowledge, no recent studies have compared relative costs in the American health care system, however. Placement of a TPC requires an upfront operative cost but is associated with a low postplacement cost;

TABLE 1: Search Terms and Results of the Searches Used

Keywords	No. of Citations	No. of Citations Reviewed	No. of Journal Articles Read
Cost effect and ascites	44	11	6
Cost analysis and ascites	76	14	8
Cost benefit and ascites	31	12	5
Malignant ascites and paracentesis	120	22	11
Ascites and peritoneal catheter drainage system (PleurX, CareFusion)	6	6	5
Ascites and tunneled catheter	14	9	9

therefore, one might expect that there exists a point in time at which the cost for treatment with a TPC will intersect with the operative costs of repeated paracentesis. The goal of this study is to determine the point in time at which TPC placement becomes less costly than repeat large-volume paracentesis (LVP).

Materials and Methods

Literature Search

The PubMed database, Excerpta Medica dataBASE, and UpToDate clinical decision support resource were used to conduct a search of the literature for articles on LVP and TPC placement, to determine the protocols for care, the rates of major complications and how such complications are treated, and the costs associated with protocols and treatments. Another goal of the literature search was to identify previously published cost-related studies associated with ascites management. The search was restricted to English-language articles, but no other search limitations were used, including limiting the search to a specific time frame. Article abstracts and summaries were reviewed if their title was relevant to ascites management in human subjects. After this review was performed, the article was read in full if information pertinent to the aforementioned criteria could be obtained. Published articles were read in full if the abstract did not exclude the data pertinent to the modeling process used. The primary data referenced in these articles but not otherwise discovered via database query were also reviewed for pertinence and for possible inclusion in the model. Table 1 lists the search terms used, the search results, and number of abstracts and articles read.

Standard Cost Calculations

Costs were determined from the payer perspective. Costs of paracentesis and TPC placement were based on 2013 Medicare allowable reimbursement rates (based on the geographic practice cost index for Colorado). The incidences of specific complications were calculated on the basis of the data obtained during the literature search. These complications were assigned associated costs on the basis of allowable reimbursement in accordance with the geographic practice cost index. If coding and reimbursement based on the geographic practice cost index were not applicable, then standard costs were calculated using online searches for shelf price.

Model Design

A decision tree–based hybrid Markov chain Monte Carlo model was built using Excel software with Visual Basic for Applications programming language (version 11, Microsoft), to answer the question of when TPC placement becomes less costly than repeat LVP (Fig. 1). Other

TABLE 2: Standard Event Costs and Explanations

Model Event	Event Cost	Event Cost Explanation
LVP	$501.43	$501.43[a] was for GPCI-adjusted reimbursement for billing code 49083 (paracentesis with imaging), $106.35 was for professional charges, and $395.08 was for technical charges
LVP-related infection treated with antibiotics	$84.05	$84.05[b] was for ofloxacin (400-mg tablets given orally every 12 hours for 7 days)
LVP-related development of loculations	$0	No additional financial effect was included in the model
LVP-related pain treated with additional medication	$18.40	$18.40[b] was for 30 tablets of oxycodone (5 mg)
TPC placement or replacement	$2442.03	$2442.03[a] was for GPCI-adjusted reimbursement for billing code 49418 (placement of a tunneled catheter), $227.95 was for professional charges, and $2214.08 was for technical charges
End-of-cycle (10-day) TPC cost	$224.63	$44.93[a] was charged per 1-L bottle, based the basis of a price of $449.26 for a package of 10 bottles (found through an Internet search); 0.5[c] bottles were used per day for 10[c] days
TPC removal	$2127.93	$2015.61[a] was charged for GPCI-adjusted reimbursement for billing code 49422 (removal of a tunneled catheter), $377.12 was for professional charges, $1638.49 was for technical charges, and $112.32 was the cost of half-cycle TPC placement
TPC-related dehydration treated with IV fluids	$6.99	$6.99[b] was for a 1-L IV bag of normal saline
TPC-related infection treated with antibiotics	$243.63	$19.26[b] was for cephalexin (500-mg capsules given orally every 12 hours for 7 days)
TPC-related infection treated with antibiotics and catheter removal	$2211.98	$2127.93 was for TPC removal, and $84.05[b] was for ofloxacin (400-mg tablets given orally every 12 hours for 7 days)
TPC dislodged but not replaced because of ascites resolution	$112.31	$112.32 was for the cost of half-cycle TPC placement
TPC block fixed with alteplase	$134.22	$134.22[b] was for 2 mg of an alteplase solution
TPC leak treated by use of more dressing changes	$11.19	$11.19[b] was for a box of cotton-woven dressing sponges

Note—LVP = large-volume paracentesis, TPC = tunneled peritoneal catheter, GPCI = geographic practice cost index.
[a]Univariate analysis with multipliers 0, 0.25, 0.5, 0.75, 1.25, and 1.5.
[b]Univariate analysis with multipliers 0, 0.5, 2, 5, 10, 100, and 1000.
[c]Bivariate analysis with multipliers 0.2, 0.4, 0.6, 0.8, 1.2, 1.4, 1.6, 1.8, 2, 2.2, and 2.4.

than the costs associated with the operative procedures, the other major events expected to influence costs for patients undergoing LVP included bacterial peritonitis treated with antibiotics, increased pain requiring additional prescriptions, and development of loculations. Major events expected to influence costs for patients receiving a TPC included dehydration, infections requiring antibiotics with or without drain removal, development of loculations, acute leaks, and catheter malfunctions requiring intervention. The methods for calculating costs associated with events

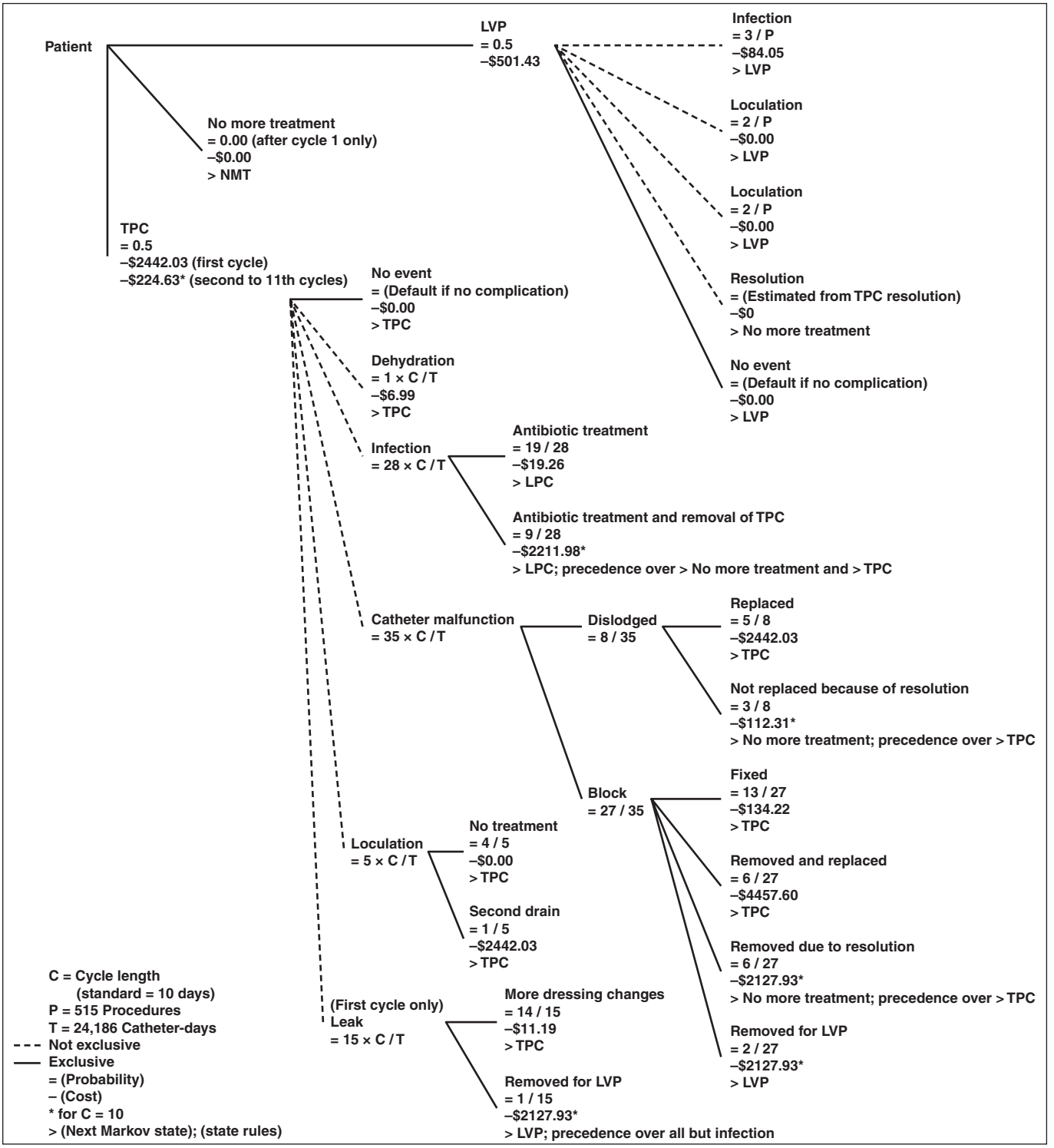

Fig. 1—Markov chain Monte Carlo model decision tree. Patients were simulated for 11 cycles each and were grouped according to initial treatment decision (large-volume paracentesis [LVP] vs tunneled peritoneal catheter [TPC] placement). Four thousand patients were simulated for each set of trial conditions. Event probabilities and costs are listed for standard trial. Variable values were changed for bivariate and trivariate analysis. Total of 1.9 million patients were simulated. Virgule constructs denote comparative incidence of assignments (patients) to each pathway at the decision nodes.

TABLE 3: Literature-Based Event Probabilities for Tunneled Peritoneal Catheters (TPCs)

Parameter	Akinci et al. [17]	Lungren et al. [18]	Tapping et al. [19]	Iyengar and Herzog [20]	Richard et al. [21]	O'Neill et al. [22]	Rosenberg et al. [10]	Brown et al. [23]	Courtney et al. [15]	Harding et al. [24]	Gotlieb et al. [25]	McNamara [26]	All
Total no. of patients	40	188	28	3	10	24	40	11	34				378
Total no. of catheter-days	3387	10,832	3152	175	700	1210	3046	300	1386				24186
Dehydration				1									1
Infection treated with antibiotics	7	1	5			3		1	2				19
Infection treated with TPC removal; start LVP	2	3				2	1		1				9
Dislodged TPC replaced	1		4										5
Dislodged TPC not replaced	2				1								3
TPC block fixed	1				1				11				13
TPC block with replacement		5							1				6
TPC block with removal; no LVP				1	2				3				6
TPC block with removal; start LVP									2				2
Asymptomatic loculations	3						1						4
Loculations; second drain placed								1					1
Early leak; functional drain		4	3						7				14
Early leak; drain removed; start LVP							1						1
Total no. of patients who underwent an LVP procedure							67			18	15	44	144
Total no. of LVP procedures							392			40	35	48	515
Infection treated with antibiotics							3						3
Development of loculations							2						2
Treatment of increased pain												7	7

Note—LVP = large-volume paracentesis.

are presented in Table 2. Complication probabilities were calculated using the incidence of events noted in the literature per total number of catheter-days, for TPC placement, and per total number of procedures performed, for LVP [10, 15, 17–26].

This model was designed to simulate 11 cycles of 400 patients. These simulations were repeated 10 times, for a total of 4000 subjects per trial. Twenty trials using a set of standard variable values based on cost calculations and event probabilities found in the literature were used to validate the model, with statistical significance denoted by $p = 0.05$. A single trial using these standard variable values was used to establish the standard trial for subsequent bivariate and trivariate analyses. Patients were grouped according to initial treatment decision (repeat paracentesis vs TPC placement), and the total cost at the end of each 10-day cycle was calculated. The point in time at which TPC placement became less costly than repeat paracentesis was determined. An additional trial in which the cost of all complication-related events was set at $0 was also performed; in other words, the only costs factored into the simulation in this additional trial were the costs of the LVP procedure, TPC placement, and the TPC bottles used for drainage.

Bivariate and trivariate analyses were conducted via additional simulations involving 4000 subjects, to detect changes in the intersection of costs for TPC placement and LVP. For bivariate analysis of total volume drained per cycle and cycle length, known as cycle-specific dynamic variables, the standard value of these variables was multiplied by adjustment factors of 0.2, 0.4, 0.6, 0.8, 1.2, 1.4, 1.6, 1.8, 2.2, and 2.4. Trivariate analysis of these variables tested each combination of adjustment factors used in the bivariate analysis.

Bivariate analyses of the LVP procedure, TPC placement, TPC removal, and bottle costs included adjusted cost factors of 0, 0.25, 0.5, 0.75, 1.25, and 1.5. Bivariate analysis for nonbillable complication-related costs included adjusted cost factors of 0, 0.5, 2, 5, 10, and 100. Analysis of the probabilities of complications was performed for each of the terminal and nonterminal events in the model; for example, the events known as "TPC infection (all)" and "TPC infection treated with antibiotics" underwent separate bivariate analyses. Bivariate analysis of these probabilities included nine adjusted probability factors spaced evenly throughout the corresponding 95% CI. The 95% CI was calculated using the Newcombe method [27], as it was applied to the total reported number of events per total number of catheter-days divided by the number of LVP procedures found in the literature. The resulting TPC-LVP cost intersection in these variant simulations was compared with that in the standard trial.

Results

Model Validation

The probability of major events, as based on a review of the literature, is presented in Table 3; these event probabilities were used in the Markov chain Monte Carlo model. Daily probabilities were assigned according to the total reported number of events per total number of catheter-days, and the daily probability was multiplied by the cycle length, to calculate the event probability per cycle. The event frequency output of 20 standard trials was compared with input parameters, to test the validity of the model. The *p* values for the individual variables ranged from 0.0684 to 0.0954, with none of the values reaching a statistically significant deviation from input, thereby confirming the validity of the model (Table 4).

TABLE 4: Anticipated (Input) Event Probabilities Versus Simulated Results From 20 Standard Trials

Event	Input	Output, Mean (± SD)	*p*
LVP infection	5.83×10^{-3}	$5.73 \times 10^{-3} \pm 4.02 \times 10^{-4}$	0.303
LVP loculation	3.88×10^{-3}	$3.75 \times 10^{-3} \pm 3.54 \times 10^{-4}$	0.101
LVP pain	1.36×10^{-2}	$1.38 \times 10^{-2} \pm 7.44 \times 10^{-4}$	0.237
LVP ascites resolution	3.72×10^{-3}	$3.73 \times 10^{-3} \pm 4.36 \times 10^{-4}$	0.954
TPC dehydration	4.13×10^{-5}	$4.09 \times 10^{-5} \pm 1.16 \times 10^{-5}$	0.868
TPC infection with antibiotics	7.86×10^{-4}	$7.68 \times 10^{-4} \pm 5.68 \times 10^{-5}$	0.188
TPC infection with catheter removal; start LVP	3.72×10^{-4}	$3.73 \times 10^{-4} \pm 4.37 \times 10^{-5}$	0.933
TPC dislodged and replaced	2.07×10^{-4}	$2.09 \times 10^{-4} \pm 2.60 \times 10^{-5}$	0.670
TPC dislodged and not replaced; no more treatment	1.24×10^{-4}	$1.25 \times 10^{-4} \pm 2.49 \times 10^{-5}$	0.830
TPC blocked and fixed	5.37×10^{-4}	$5.22 \times 10^{-4} \pm 4.29 \times 10^{-5}$	0.129
TPC blocked, removed, and replaced	2.48×10^{-4}	$2.54 \times 10^{-4} \pm 4.35 \times 10^{-5}$	0.519
TPC blocked, removed, and not replaced; no more treatment	2.48×10^{-4}	$2.57 \times 10^{-4} \pm 3.74 \times 10^{-5}$	0.308
TPC blocked and removed; start LVP	8.27×10^{-5}	$9.24 \times 10^{-5} \pm 2.39 \times 10^{-5}$	0.0848
TPC asymptomatic loculation	1.65×10^{-4}	$1.76 \times 10^{-4} \pm 2.55 \times 10^{-5}$	0.0684
TPC loculation; second drain placed	4.13×10^{-5}	$3.90 \times 10^{-5} \pm 1.37 \times 10^{-5}$	0.453
TPC leak treated with more dressing	3.60×10^{-2}	$3.50 \times 10^{-2} \pm 4.00 \times 10^{-3}$	0.280
TPC leak treated with removal; start LVP	2.57×10^{-3}	$2.30 \times 10^{-3} \pm 1.20 \times 10^{-3}$	0.318

Note—Input is based on probabilities found in the literature. LVP = large-volume paracentesis, TPC = tunneled peritoneal catheter.

Standard Trial Simulation

Simulated patients were assigned to an LVP group or a TPC placement group, on the basis of a treatment decision made on day 0 (i.e., day of treatment decision), and the average costs at the end of each cycle were calculated for each of the 10 simulations of 400 patients. A second simulation included only the costs for the LVP procedure, TPC placement or removal, and TPC bottles used for drainage, with all other events set to a cost of $0. On the basis of these results, the cost curves cross at 82.8 days (SD, ± 3.6 days; range, 75.8–89.6 days), as calculated from the 10 component simulations. This compares to a mean cost intersection of 74.3 ± 1.5 days (range, 71.9–77.3 days) when all complication costs were removed. The results of these two trials are displayed with trend lines in Figure 2.

Bivariate Analysis

The TPC-LVP cost intersections resulting from bivariate analysis of the cycle-specific dynamic variables (volume drained per cycle and cycle length) are displayed in Figure 3, and those resulting from trivariate analysis are displayed in Figure 4. Although cost intersection occurred at later dates, with increases noted in both of these variables, changes in volume drained per cycle had a more exponential effect. Although not displayed in Figure 4, when the volume drained

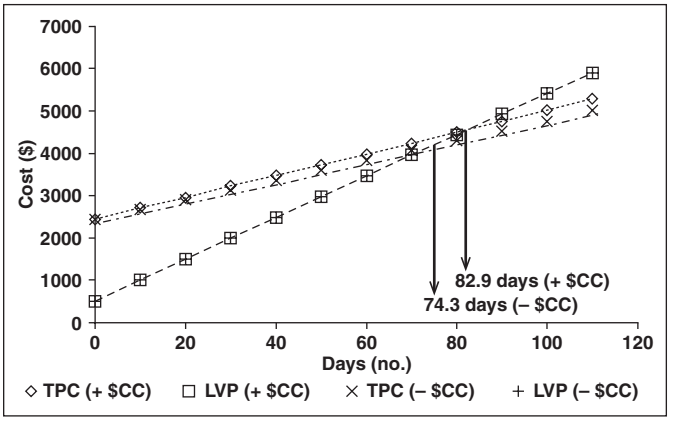

Fig. 2—Per-patient cost versus time for tunneled peritoneal catheter (TPC) placement and large-volume paracentesis (LVP). Intersection occurred at 82.9 days when complication-related costs were included in model and at 74.3 days when these costs were removed. After this intersection, cost advantage of TPC increases with time. Slopes are as follows: TPC + complication-related costs ($CC) = $25.8 per day; LVP + $CC = $49.0 per day; TPC – $CC = $23.2 per day; LVP + $CC = $49.1 per day. LVP-per-cycle cost points and resulting trend lines overlap for simulations with and without complication costs factored into model.

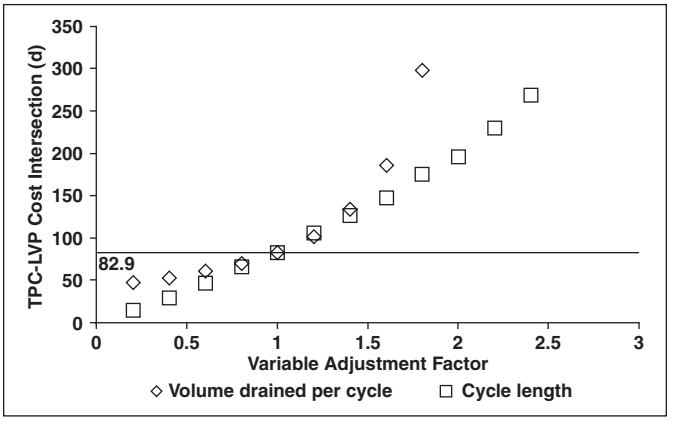

Fig. 3—Resulting tunneled peritoneal catheter (TPC)–large-volume paracentesis (LVP) cost intersection after bivariate analysis of cycle-specific dynamic variables of volume drained per cycle and cycle length. Increases in both variables result in cost intersection at later point in time, and volume drained per cycle has more exponential effect. Axis is drawn at cost intersection (82.9 days) for standard trial.

TABLE 5: Beta Values and Standardized Beta Values for Variables After Bivariate Analyses

Variable Analyzed	Beta Value	Standardized Beta Value
Cycle dynamics		
Volume drained per cycle	366.7	5.27
Cycle length	111.6	1.32
Intrinsic costs		
TPC cycle	68.1	0.65
TPC placement	107.0	1.25
LVP cycle	–25.6	–0.81
Complication-related costs		
TPC-LVP infection (antibiotics)	–0.1	–0.41
LVP pain	–0.1	–0.41
TPC removal	5.1	–0.33
TPC dehydration	0.0	–0.41
TPC infection (antibiotics only)	0.1	–0.41
TPC block	0.3	–0.40
TPC leak	0.0	–0.41
Probabilities		
Ascites resolution (all)	6.0	–0.31
LVP complication (all)	12.7	–0.21
LVP infection	–21.8	–0.75
LVP loculation	1.4	–0.39
LVP pain	8.6	–0.27
LVP resolution	38.1	0.18
TPC complication (all)	15.7	–0.17
TPC dehydration (all)	–11.5	–0.59
TPC infection (all)	20.3	–0.09
TPC antibiotic treatment	8.8	–0.27
TPC antibiotic treatment and removal	55.0	0.44
TPC malfunction (all)	52.1	0.40
TPC dislodge (all)	9.4	–0.26
TPC dislodge and replaced	22.5	–0.06
TPC dislodge and not replaced	–28.4	–0.85
TPC block (all)	38.2	0.18
TPC block and fix	6.3	–0.31
TPC block and replaced	62.9	0.57
TPC block and removed (no more treatment)	16.9	–0.15
TPC block and removed (LVP)	27.5	0.02
TPC loculation (all)	8.3	–0.28
TPC loculation no treatment	–1.0	–0.42
TPC loculation and second drain	17.2	–0.14
TPC leak (all)	5.1	–0.33
TPC leak with dressing	3.5	–0.35
TPC leak and removed (LVP)	–6.7	–0.51

Note—Beta values were calculated as the slope of the tunneled peritoneal catheter (TPC)–large-volume paracentesis (LVP) intersection versus the variable adjustment factor during univariate analysis. Standardized beta values were calculated by subtracting the mean of the beta values and dividing by the standard error.

was increased by a factor of 2 (10 L per cycle) the intersection was extended to 1120 days, and increases by factors of 2.2 and 2.4 prevented cost intersection.

Intersections resulting from bivariate analysis of intrinsic cost variables are shown in Figure 5. These costs are incurred regardless of complication, and they include the TPC cycle cost associated with the use of bottles, TPC placement cost, and LVP cycle cost resulting from the paracentesis procedure. TPC cycle cost had an exponential effect on cost intersection; when this cost was set to $0, intersection occurred at 42.7 days.

Intersections resulting from bivariate analysis of complication-related costs are shown in Figure 6. These include costs of interventions for TPC infection without catheter removal, LVP infection or TPC infection requiring catheter removal, TPC-related dehydration, TPC-related block, TPC-related leak, LVP-related pain, and TPC removal. With the exception of costs for TPC removal, when costs associated with complications were removed or increased by a factor of 10, the resulting intersections did not depart from the 80- to 90-day range. Increasing costs by a factor of 100 resulted in an intersection at 91.8 days for TPC infection without catheter removal, 78.8 days for nonprocedural costs (i.e., everything but the removal cost) associated with TPC infection treated with removal of catheter and LVP-associated infections, 117 days for TPC-related catheter blocks, and 74.9 days for LVP-associated pain. Changing the cost of TPC removal by factors of 0 and 0.25 resulted in intersections at 78.0 and 79.1 days, respectively.

All cost intersections resulting from bivariate analysis of complication probabilities on the basis of their respective 95% CIs, as determined using the Newcombe method [27], are shown as a cloud in Figure 7. Of note, all intersections occurred within a range of 80.4–89.5 days, and none was greater than 2 SDs from the intersection in the standard trial (75.6–90.2 days).

Standardized beta weights were calculated for each variable analyzed in the model. This was achieved by calculating the beta value for individual bivariate analyses. The beta value was defined as the slope between positive-output TPC-LVP intercept values and the corresponding input variable factor. The beta values were standardized by subtracting the mean of beta values and dividing by the standard error. The results of these calculations appear in Table 5.

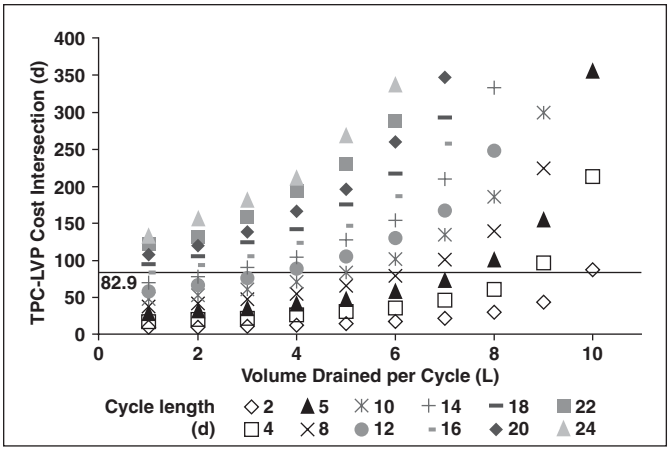

Fig. 4—Resulting tunneled peritoneal catheter (TPC)–large-volume paracentesis (LVP) cost intersection after trivariate analysis of cycle-specific dynamic variables of volume drained per cycle and cycle length. Variables were tested in combinations to assess effect on resulting cost intersection. These combinations better reflect those that may be observed in practice. Axis is drawn at cost intersection (82.9 days) for standard trial.

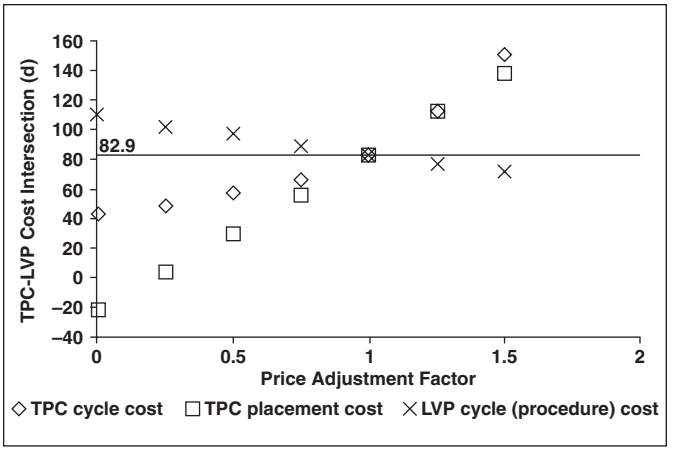

Fig. 5—Resulting tunneled peritoneal catheter (TPC)–large-volume paracentesis (LVP) cost intersection after bivariate analysis of intrinsic cost variables of TPC cycle cost, TPC placement cost, and LVP cycle cost. These represent vacuum bottle cost, TPC procedural cost, and paracentesis procedural costs, respectively. TPC-related costs have greater influence on cost intersection, and intersection occurs at 42.7 days when TPC cycle cost is reduced to $0. Axis is drawn at cost intersection (82.9 days) for standard trial.

Discussion

The treatment of refractory ascites is complex, but it typically centers around repeat paracentesis procedures. Malignant ascites appears to arise from a process that is more complex than the process associated with benign ascites. The process involves decreased lymphatic drainage and increased vascular permeability; the result is an ascitic fluid with positive cytologic findings, high protein and cytokine levels, and a low serum–ascites fluid albumin gradient [1–6]. Ascites draining is further complicated in some patients because decreased circulating volume triggers activation of the renin-angiotensin-aldosterone system, resulting in sodium retention [2–6]. It is perhaps because of this complex pathophysiologic profile that traditional medical management with diuretics and salt restriction is rarely effective for patients with malignant ascites, and it may be why more invasive techniques are frequently required for palliation [1–8].

Peritoneovenous shunting is one alternative technique used for cirrhosis that has also been used in patients with malignant ascites, to relieve the need for repeat paracenteses [28]. It is reserved only for very select patients because it is considered to be associated with worse efficacy and more complications than paracentesis; these complications include disseminated intravascular coagulation, tumor seeding, and a higher mortality rate [1–6, 10, 12–16, 19]. In many instances, a more favorable option is the use of a TPC that allows patients to drain ascitic fluid on their own at home. In general, when these long-term catheters have been used, both the complication rate and efficacy are similar to those seen with repeat paracentesis [10].

The modeling process used in this study was performed both to provide a range of results based on the wide distribution of primary data collected from the literature review and to make the results more generalizable from one institution to another by providing these ranges of results. Modeling in such a way also minimizes potential skewing of the data by minimizing the effect of outlier data points, which is a significant risk associated with simply using the mean or median values presented in the literature.

Specifically, the decision to use a Markov chain Monte Carlo model when simulating this population was based on the recognition that some patients who start treatment with TPC placement will eventually need to have their catheters removed for management with LVP or because of ascites resolution. The variability with which such a transition would occur (e.g., on the 10th day vs on the 100th day) results in significant cost differences. The permutations of such variability make the Markov chain Monte Carlo method, in particular, a more appropriate solution than attempting to write an equation to calculate when the costs of treatment would intersect. As shown by the simulation in which complications were excluded, simple equations that take into account only the intrinsic costs (i.e., LVP procedure vs TPC procedure and bottles) could be used to estimate cost crossover, but they may potentially result in a significant underestimation that favors use of the TPC. For further discussions of the modeling process, the reader is referred to excellent articles by Sonnenberg and Beck [28], Hunink et al. [29], and Rochau et al. [30].

According to the results of this Markov chain Monte Carlo simulation, the cost curves for use of the TPC versus LVP cross at 82.8 days for patients simulated to drain 5 L of ascitic fluid every 10 days. When the LVP that occurs on day 0 is included, these results indicate that the cost curves intersect between the ninth and 10th LVP procedures (i.e., TPC placement becomes less costly for patients expected to require LVP a total of 10 or more times). The intersection of these cost curves occurred earlier (between the eighth and ninth LVP procedures performed) when the model was adjusted to evaluate treatment from a payer perspective that included only the costs associated with TPC placement, TPC bottles, and LVP procedural costs.

Although the study does not directly include death in this model, this was intentional. There are reports of LVP-associated death [30, 31]; however, the only study comparing deaths associated with LVP versus those associated with TPC placement showed no difference between the two [10]. The focus of this model was instead to offer guidance regarding cost crossover relative to the estimated life expectancy of a patient. According to bivariate analyses, the cycle-specific dynamic variables of volume drained per cycle and cycle length, which were meant

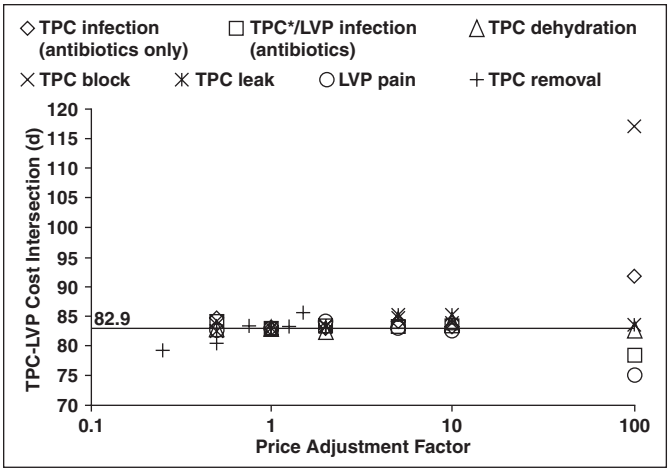

Fig. 6—Resulting tunneled peritoneal catheter (TPC)–large-volume paracentesis (LVP) cost intersection after bivariate analysis of complication-related cost variables. Axis is drawn at cost intersection (82.9 days) for standard trial. Although points are difficult to discriminate because of overlap, all tested price adjustments are plotted here. With exception of TPC removal cost, only when prices were adjusted to 100 times greater than standard assigned value did deviation from range of 80–90 days occur. Asterisk denotes that nonprocedural cost associated with TPC infection requiring removal of catheter was same as cost assigned to treatment of LVP-associated infection.

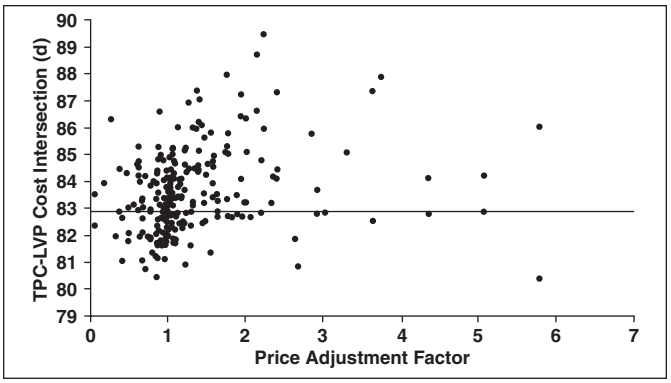

Fig. 7—Resulting tunneled peritoneal catheter (TPC)–large-volume paracentesis (LVP) cost intersection after bivariate analysis of complication probabilities. Points are plotted as single series but represent bivariate analysis for all complication probabilities used in model. All resulting TPC-LVP cost intersections occurred within range of 80.4–89.5 days.

to represent patient-specific ascites-related variables, had the most influence on cost intersection for the two treatment modalities. The results of trivariate analysis of these two variables might be most useful for clinicians considering the cost implications of TPC placement in their unique patients. Under the assumption that the procedural and bottle costs are similar to those used in this simulation, providers would be able to chart the average paracentesis interval and volume of fluid drained per paracentesis procedure into the graph shown in Figure 4, to obtain a general idea of when the cost curves would cross for a given patient. If life expectancy is greater than this intersection, then the patient could expect to derive a cost advantage from TPC placement. Furthermore, this cost advantage would be greater for patients with a larger difference between the cost intersection and life expectancy.

Placement of a TPC provides an even earlier and greater cost advantage for patients who undergo paracentesis on a more frequent basis or who have less than 5 L of fluid drained per procedure. Methods that reduce the daily costs associated with TPC placement—such as the ability to drain ascites without the use of bottles—also greatly improve the cost advantage associated with TPC placement. In determination of whether TPC placement would reduce costs relative to the continued use of LVP for ascites management, complications have the least influence on the relative cost of these two modalities.

Limitations

The limitations of this study stem from the underlying assumptions used in the simulation. One such assumption is that patients are capable of managing a TPC at home, in accordance with proper use, with no added costs (e.g., home health care nursing), relative to patients with LVP. Similarly, the model does not consider changes in the cost of transportation, wages, and other factors, which would be difficult to assign. This limitation is somewhat addressed in the bivariate analysis, in which changes in cost intersection versus TPC and LVP cycle costs are examined. The model also assumes that collection of ascitic fluid occurs at a rate independent from frequency of drainage. The usefulness of the model depends on the predictability of the length of time between paracentesis and volume accumulation; however, intrapatient intervals may be variable. It may be difficult to estimate an average, or the estimation may lack validity for predicting future paracentesis intervals for some patients.

Another limitation of this study is the small sample size found in the literature and used in construction of the model. The method used for assignment of TPC-related event probabilities treated as a single proportion the total number of reported events and the total number of catheter-days found in the literature, to prevent overweighting of smaller studies. Similarly, probabilities of LVP-related events were assigned on the basis of the total incidence of events per the total number of procedures. The Newcombe method was thus used to construct the 95% CI, because it is meant for single proportions. Although the adjustment factors selected by use of this method for bivariate analysis of complication-related costs and probabilities may have failed to capture the true value for these variables, comparison of standardized beta values suggests that these variables had the least influence on cost crossover. The complications associated with the largest beta values were those related to infection or catheter malfunction, but the risk of these complications was assigned on a cycle-by-cycle basis, with no change in risk noted for patients who experienced prior infection or malfunction. Thus, this simulation may not accurately represent patients who have an increased predisposition for catheter malfunction or infection, such as patients undergoing chemotherapy. Adjustments could be made to consider such patients, but because evidence in the literature is limited in this regard, the model attempts to reflect the best available evidence.

It is also important to note that this study is an economic study and not a cost-efficiency study. The latter would consider comfort and quality when assessing life differences between patients receiving the two treatments, but data of this nature are currently lacking. Decision-making algorithms would likely im-

prove with future research investigating how TPC placement and LVP affect quality of life in patients with malignant ascites.

Conclusion

For patients with refractory malignant ascites, LVP becomes more costly once the procedure is performed between nine and 10 times or at approximately 83 days after initiation of paracentesis, if paracentesis is repeated every 10 days, with 5 L removed each time. TPC placement has an improved cost advantage for patients with longer life expectancy, those who undergo paracentesis more frequently, or those who have less fluid drained per procedure.

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