Factors associated with the high cost of liver transplantation in adults

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Objectives: To determine the overall direct cost of liver transplantation in Canadian adults and to identify the factors that are associated with high cost. **Methods:** The direct cost of liver transplantation from the perspective of third-party payers was determined in a retrospective analysis of data from hospital charts and databases. A consecutive series of 119 adults who underwent liver transplantation between 1991 and 1992 was followed from the date of listing for transplantation to the second anniversary of the transplant. Patient-specific services during the pre-transplantation, transplantation and post-transplantation phases were compiled and costed. The primary consideration was the impact of complications on the cost of transplantation. Secondary considerations were the impact of age, sex of the patient, diagnosis and severity of liver disease on the total cost. **Results:** The overall mean measured cost of liver transplantation was Can$89 066 (range from Can$30 505–Can$690 431). The multivariate logistic regression model for overall costs revealed that severe liver disease (OR = 11.97), cytomegalovirus infection (OR = 6.12), additional operative procedure (OR = 4.22) and biliary complications (OR = 5.00) were associated with an increased likelihood of high cost. The addition of services that were not measured in the present analysis increased the total overall cost to a mean of $121 732 (1998 Canadian dollars, follow-up costs discounted and inflation adjusted). **Interpretation:** The factors that were associated with high cost of liver transplantation in Canadian adults were advanced liver disease, postoperative cytomegalovirus infection, the requirement for additional operative procedures and biliary complications.

Objectifs : Déterminer le coût direct global d'une transplantation de foie chez les adultes du Canada et cerner les facteurs associés au coût élevé. **Méthodes :** On a calculé le coût direct d'une transplantation de foie du point de vue des payeurs tiers dans le contexte d'une analyse rétrospective de données tirées de dossiers d'hôpital et de bases de données. On a suivi une série de 119 adultes consécutifs ayant subi une transplantation de foie entre 1991 et 1992, depuis la date de leur inscription pour une transplantation jusqu'au deuxième anniversaire de la transplantation. On a compilé les services particuliers reçus par les patients avant, pendant et après les phases de la transplantation et l'on en a établi le coût. Le facteur principal a été l'impact des complications sur le coût de la transplantation. Les facteurs secondaires ont été l'impact de l'âge, du sexe du patient, du diagnostic et de la gravité de l'hépatopathie sur le coût total. **Résultats :** Le coût moyen global mesuré d'une transplantation de foie s'est établi à 89 066 $CAD (intervalle de 30 505 à 690 431 $CAD). Le modèle de régression logistique à variables multiples des coûts totaux a révélé un lien entre une hépatopathie grave (CP = 11,97), une infection par le cytomégalovirus (CP = 6,12), une intervention supplémentaire (CP = 4,22) et des complications biliaires (CP = 5,00) et une probabilité accrue de coût élevé. L'ajout de services que l'on n'a pas mesurés au cours de l'analyse en cause a porté le coût global total à une moyenne de 121 732 $ (dollars canadiens de 1998, total corrigé des coûts de suivi et de l'inflation). **Interprétation :** Une hépatopathie avancée, une infection postopératoire par le cytomégalovirus, l'obligation de procéder à des interventions supplémentaires et les complications biliaires sont au nombre des facteurs associés au coût élevé d'une transplantation de foie chez les adultes du Canada.

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The factors that affect the cost of liver transplantation are largely unknown. The extent to which preoperative and postoperative factors could be used to predict costs is relevant to the allocation of health care resources. The cause and severity of liver disease, as well as postoperative complications, may be predictive of overall costs. The present analysis was an attempt to determine the overall direct cost of liver transplantation in Canadian adults from the perspective of the Government of Ontario and to identify the factors that are associated with high cost.

Liver transplantation is the only form of treatment available for end-stage liver disease (ESLD).[1] Approximately 350 patients receive liver transplants per year in Canada. One-year survival rates as high as 93%,[2] 88%[3] and 83%[4] have been reported after liver transplantation. Canadian institutions have reported similar results. The Canadian Organ Replacement Registry has reported a 1-year survival of 85% and a 5-year survival of 74%.[5] Some of the costs of liver transplantation are available, but most studies report transplant charges, with very little consideration of actual costs of the procedure.[6,7] The factors associated with improved prognosis after liver transplantation have been documented by several studies.[8,9] However, the impact of these factors on the cost of treatment is unknown. The identification of groups in whom liver transplantation is particularly expensive may permit more informed decision-making, especially when combined with effectiveness data. Determination of the cost of complications may lead to strategies to reduce those complications that are particularly expensive. In addition, the data on costs as they relate to severity of liver disease will aid decision-making on the timing of transplantation. The ultimate goal will be to improve resource allocation.

Methods

The study was a retrospective analysis using existing data from hospital charts and databases. A consecutive series of patients who underwent liver transplantation was followed longitudinally from the date of placement on the transplant waiting list until 2 years had elapsed from the date of transplantation. Data were obtained on all adults who underwent primary liver transplantation at Toronto General Hospital in 1991 and 1992.

The viewpoint of the analysis was the Ontario Ministry of Health, which funds medical care for all legal residents of Ontario. This viewpoint was chosen because the main area of interest was the differential costs associated with patient-specific factors, such as diagnosis, severity of liver disease, patient age and sex and postoperative complications. The costs that were included were the costs of services provided in hospital, including medications, tests, operating room (OR), recovery room, ward and intensive care unit costs, and professional fees. These costs were calculated for the pre-transplantation, transplantation and post-transplantation periods, and for overall costs.

Data were obtained from a systematic review of hospital charts and existing clinical databases. All data regarding clinical services provided to 119 adult primary liver transplant recipients at Toronto General Hospital in 1991 and 1992 were assembled. The liver transplant database maintained by the Gastrointestinal Transplant Service contained patient demographic information, as well as diagnosis, severity of liver disease, specifics of the transplant operation, complications and survival. Data on some laboratory services, blood products and medication unit costs were available as parts of databases maintained by laboratory services, the blood bank and the pharmacy. Professional medical fees received by physicians were obtained from the departments of surgery, medicine and anesthesia. Data were manually extracted from the hospital inpatient charts to obtain information on length of stay, hours in the OR, use of the perfusionist and of the recovery room, many laboratory tests, radiologic investigations, medication use and consultations with those physicians not captured from the departmental data.

The method used to calculate the cost of services for individual patients is described in the *Ontario Guide to Case Costing*.[10] The method divides the hospital into individual functional centres, each of which generates a functional centre detailed report (FCDR) containing budgetary and workload details. Functional centre unit costs have been determined from the FCDRs by dividing the total actual expenditure of the functional centre by the number of services provided (i.e., number of tests performed, total number of inpatient days on the ward). The simultaneous equation allocation method was used to allocate overhead costs at Toronto General Hospital (H. Bolley, Health Administration, University of Toronto: unpublished data, 1992), and the resulting overhead adjustment factors were used in the present analysis.

As recommended, medication costs were tracked and assigned directly to the patient[6] and were therefore excluded when calculating functional centre unit costs. The exact amount of each drug that each patient received was abstracted manually from the medication records on the inpatient hospital charts at Toronto General Hospital. The hospital pharmacy provided a list of every drug in the formulary, with the costs charged to the patient wards for each drug. These charges did not vary through the study period. The relevant drugs were extracted from the formulary list, and prices were converted to unit costs, which in most cases was dollars per milligram of drug. Costs for all drugs for each patient during each of the 3 phases (pre-transplantation, transplantation and post-transplantation) were calcu-

lated. Gancyclovir and OKT3 were used as markers to identify patients with cytomegalovirus (CMV) infection and severe rejection, respectively.

The number of hours of OR time that each transplantation consumed was extracted from the OR record on the inpatient hospital chart. When patients returned to the OR for further surgery, these hours were counted in the relevant treatment phase. The FCDRs for the relevant costing centres were used to calculate OR hourly costs and were appropriately adjusted for overhead. This value was multiplied by the number of OR hours for each patient treatment phase to yield total OR costs. In most cases, following the transplant operation patients were taken directly to the surgical intensive care unit. The only patients who were treated in the recovery room were those who had returned to the OR for further surgery. The relevant FCDR was used to calculate costs by dividing the total costs by the overall number of patients treated in the recovery room.

The numbers of days spent in the intensive care unit and the hospital ward were extracted from the hospital discharge record on the inpatient chart. The costs of 1 day in the intensive care unit and inpatient ward were obtained from the relevant FCDRs and adjusted for overhead.

For donors outside southern Ontario, staff from Toronto General Hospital were flown by chartered plane to the location of the donor. The cost of air transport for each donor run was obtained directly from Skycharter (Mississauga, Ont.) who provided the actual amount charged to the Ontario government for each trip. To this was added the cost of 2 OR hours, plus a 12-hour stay in the intensive care unit. These numbers were estimates of the time it takes the retrieval team to do the donor procedure, and the time between the declaration of brain death and the actual donor operation. The costs calculated as above for Toronto General Hospital were used to estimate the costs of these services in all hospitals.

The Multiple Organ Retrieval and Exchange (MORE) program paid for all administrative costs related to transplantation. This included staff costs related to coordination, planning and retrieval. For donors in southern Ontario, in most cases ground transportation was used for retrieval, which came out of the budget for the MORE program. Donor surgical supplies, tubing and organ preserving equipment and solutions were also included. The mean cost for each donor was used in the present analysis.

The actual amount paid to surgeons, anesthetists, hepatologists and intensivists were obtained directly from relevant offices. For other physicians, consultations were noted from the individual chart reviews. The payments made to the consultants were determined from the Schedule of Benefits of the Ontario Health Insurance Plan that was in effect at the time.[11] It proved difficult to obtain complete billing data from the radiology department, so some payments made to radiologists may have been missed.

The number of many of the tests performed on each patient was obtained from the charts. The hospital maintains a database of tests carried out on all patients. However, for the period under consideration, only hematology, microbiology and radiology services were included in the database. The costs of provided services were calculated from workload unit costs. Workload unit costs were determined from the FCDRs for each relevant laboratory. The number of workload units required for each test were extracted from the *Management Information System Guidelines*.[12]

The total cost of each phase of the transplantation process was calculated by adding the costs of each of the services. The total cost for each of the 3 phases was then added to provide the overall measured cost for each patient.

In the second phase of our overall costing process, estimates were made of the cost of many of the services that were not measured. The mean cost of work-up, pre-transplantation care and post-transplantation care had been determined from Toronto General Hospital actual program data as part of the Joint Policy and Planning Committee project.[13] The cost of the residents and interns was estimated using the pay rates for postgraduate trainees.[14]

Some services provided to these patients were not measured or estimated. The hospital costs not included were those associated with the services of allied health professionals, such as physiotherapy, occupational therapy and social work. The costs to the health care system not provided at The Toronto Hospital have also been missed. However, the patients normally were transferred to Toronto General Hospital when serious illness developed. Other costs not included were those borne by the patient, time lost from work, intangible costs such as psychic costs to the patients and families, and changes in the quality of life of patients and their families.

The main purpose of the current study was to compare costs between patients treated in a relatively short time. Therefore, issues of discounting and inflation adjustment have not been emphasized. However, in the estimation of the overall cost of liver transplantation, these issues cannot be ignored. Discounting is necessary because money spent today is considered to be more valuable than money to be spent in the future. Discount rates used in the literature vary between 3% and 7%.[15] In the present analysis, 5% has been used. The costs that were incurred in 1991 were adjusted for inflation to 1998 values to permit estimation of the mean overall costs of a liver transplant in 1998. The Health and Personal Care item from the Canadian Consumer Price

Index was used to adjust 1992 costs for inflation.[16]

Statistical analysis

The relationship between total cost and clinical variables was investigated. The primary dependent variable was considered to be total cost. Independent variables were patient age, sex, diagnosis, severity of disease as indicated by status and complications. Age in decades was used as a categorical variable. The specific complications considered were CMV infection, as indicated by treatment with gancyclovir, severe rejection, as indicated by treatment with OKT3, additional surgical procedures and biliary tract complications (leaks and strictures). For these 4 complications, chart documentation was straightforward from the available markers. For other complications, such as wound infections, documentation was felt to be incomplete and unreliable. The analysis was carried out using SPSS statistical software (Version 5; SPSS Inc., Chicago).

Most of the costing data were not normally distributed. Because of the extremely skewed nature of the data, a log transformation of the data was attempted. However, the data were still unacceptably skewed, a condition that persisted even after a log-log transformation. The inability to achieve a normal distribution ruled out the use of applied linear regression models.[17] The data were separated into those above and below the median value for each variable. Patients were considered either high cost or low cost for each variable in each phase and for overall costs.

Bivariate analysis was carried out for each variable in succession. The statistical significance of cost differences was assessed with the χ^2 test and, when appropriate, the Yates continuity correction for 2×2 tables was applied. Likelihood ratios were calculated, and the Mantel–Haenszel test for linear association was carried out. For each phase, the variables that predicted high cost were identified. Multivariate logistic regression models were tested to estimate the independent effect of the above variables on cost. All of the variables were tested in stepwise regression models, using both forward and backward methods. Only those variables that remained in the final model are reported here. Prediction models for the transplantation and post-transplantation phases and for overall costs were created and evaluated. Odds ratios, 95% confidence intervals (CIs) and probability values were calculated.

Results

During 1991 and 1992, 121 primary liver transplantations were performed on adults at Toronto General Hospital. In 2 cases, hospital charts were missing and it was not possible to obtain essential data. The analysis is therefore based on 119 patients. The causes of the liver failure in these patients are shown in Table 1, along with patient demographics. The 2-year survival of liver transplantation for these 119 patients was 75.6%.

For all phases, the range in measured costs was very large and the data were extremely skewed. In most cases, the mean cost was much higher than the median. The majority of patients had very low inpatient costs during the pre-transplantation phase. A small number of patients underwent operative procedures while waiting for transplantation. The overall median cost of the pre-transplantation phase was Can$546 (mean Can$5756, range from 0–$64 108). As expected, the transplantation phase was the most expensive of the 3 phases. The overall median cost for the transplantation phase was Can$54 794 (mean Can$69 892, range from $14 353–$514 049). The median post-transplantation cost was Can$4882 (mean Can$13 418, range from $13–$171 362) (Table 2).

The mean measured total cost of all 3 phases was Can$89 066 (range from $30 505–$690 431). For all phases, and for overall costs, the largest single measured cost component was inpatient care. The mean length of stay was 43 days, consisting of 9 intensive care unit days and 34 regular ward days. The combination of intensive care unit and ward care accounted for 48.54% of the overall measured cost. Tests accounted for 13.12% of overall measured costs, and medications for 7.52% (Table 3).

Bivariate analysis, examining the relationship between each variable and overall cost showed that higher costs were observed with the following pre-transplantation variables: female sex, a diagnosis of alcoholic cirrhosis or to a lesser extent hepatitis C; age in the sixth decade; and pre-transplantation severity of illness status 3 (intensive care unit, Table 4). Higher costs were also observed with the following post-transplantation variables: presence of severe rejection; CMV infection; additional op-

Table 1

Characteristics of 119 Patients Who Underwent Liver Transplantation

Characteristic	Patients, no. (and %)*
Mean age (range), yr	45.2 (15–66)
Male sex	74 (62.2)
Severity of liver disease	
Status 1 (at home)	54 (45.4)
Status 2 (in hospital)	47 (39.5)
Status 3 (in ICU)	14 (11.8)
Status 4 (fulminant)	4 (3.4)
Primary diagnosis	
Primary sclerosing cholangitis	21 (17.6)
Hepatitis C cirrhosis	18 (15.1)
Primary biliary cirrhosis	17 (14.3)
Cryptogenic cirrhosis	17 (14.3)
Alcoholic cirrhosis	13 (10.9)
Hepatitis B cirrhosis	9 (7.6)
Autoimmune cirrhosis	4 (3.4)
Alpha-1-antitrypsin deficiency	4 (3.4)
Fulminant hepatitis	4 (3.4)
Hepatocellular carcinoma	3 (2.5)
Wilson's disease	2 (1.7)
Other	7 (5.9)

*Except where indicated
ICU = intensive care unit.

erative procedures; and biliary complications. There was no difference in cost between those who lived and those who died. Higher costs in the pre-transplantation and transplantation phases in those who died were countered by higher post-transplantation costs in those who lived.

The patients were divided into low- and high-cost groups for each phase and overall cost. For the pre-transplantation phase, none of the examined variables was associated with a statistically significant increased probability of high cost at the $p < 0.05$ level. However, for the transplantation phase, patient age in decades, sex, diagnosis, survival, postoperative CMV infection and severe rejection were not associated with high cost, whereas severity of illness status 3 or 4, additional surgical procedures and biliary complications were associated with high cost. The only variable associated with high cost in the post-transplantation phase was CMV infection. The variables that were associated with high overall cost were preoperative status 3 or 4, CMV infection, severe rejection and additional surgical procedures. Table 4 outlines the association between each of the variables and high cost in each of the phases. Those variables identified by bivariate analysis as being associated with a significantly increased probability of high cost ($p < 0.05$) have been highlighted.

Table 5 illustrates the logistic regression models for the 3 phases. For all variables in the model, the 95% CIs do not include unity, and all p values are less than 0.05, verifying statistical significance between the indicated variables and high cost. In the pre-transplantation phase, none of the examined variables was independently associated with high cost. For the transplantation phase, status 3 or 4 patients were more likely to be independently associated with a high cost than status 1 or 2 patients as were patients requiring additional surgery and patients with biliary complications. In the post-transplantation phase, only CMV infection was found to be independently associated with high cost. For overall measured cost, status 2 versus 1, status 3 or 4 versus 1, CMV infection, additional surgery and biliary complications, were all independently associated with high cost.

The contribution made by the various elements to the significant high cost variables was examined. Table 6 shows the difference in the costs of the various elements for the low- and high-cost groups for each variable in the overall measured cost that were associated with a significantly increased cost. For the cost increase noted for patients with more severe liver disease, the costs of blood products, medications and stay in the intensive care unit were the largest contributors. The patients with CMV infection had higher costs

Table 2

Median Costs (and Range of Costs in Canadian Dollars) of Liver Transplantation According to Phase (Pre-transplantation, Transplantation and Post-transplantation)

	Phase		
Cost category	Pre-transplantation	Transplantation	Post-transplantation
Donor		1 974 (1 678–24 517)	
MORE		5 110 (5 110–6 386)	
Operating room	0 (0–1 439)	4 629 (2 159–23 218)	0 (0–5 661)
Perfusion		1 284 (0–1 284)	
Recovery room	0 (0–646)	0 (0–739)	0 (0–462)
Intensive care unit	0 (0–21 121)	6 499 (0–178 713)	0 (0–68 938)
Ward	0 (0–37 900)	10 455 (0–162 054)	3 314 (0–77 542)
Drugs	0 (0–11 099)	2 591 (8–59 971)	168 (0–18 209)
Tests	809 (0–18 862)	3 724 (238–74 748)	1 515 (0–43 151)
Blood		1 386 (0–6 386)	
Surgeon		3 131 (1 014–7 143)	
Anesthesiologist		121 (131–4 744)	
Internist		530 (0–2 385)	
Overall cost	546 (0–64 108)	54 794 (14 353–514 049)	4 882 (13–171 362)

MORE = Multiple Organ Retrieval Exchange.

Table 3

Percentage Contribution of Each Category During the Three Phases to the Total Cost of Liver Transplantation

	Phase			
Category	Pre-transplantation	Transplantation	Post-transplantation	Overall
Donor		10.76		8.44
MORE		8.20		6.44
Operation room	0.45	7.43	1.87	6.14
Perfusion		0.99	0.08	0.78
Recovery room	0.18	0.02	0.09	0.04
Intensive care unit	9.15	21.30	6.05	18.20
Ward	65.38	22.08	58.35	30.34
Drugs	5.46	7.26	9.80	7.52
Tests	19.38	10.65	23.76	13.12
Blood		3.04		2.38
Surgeon		4.57		3.59
Anesthetist		2.80		2.20
Internist		0.96		0.75
Overall percentage	6.46	78.47	15.07	100.00

MORE = Multiple Organ Retrieval Exchange.

in the medications, tests, intensive care unit stay and ward stay elements, and patients with additional surgery and biliary complications had higher costs in all 5 of the examined elements.

A sensitivity analysis was done to examine the impact of changes in individual cost categories on total cost. If total inpatient costs were to be reduced by shortening the length of stay from 43 to 21 days, the total overall measured cost could be reduced by 25%. However, the mean cost of a hospital day does not take into account that the cost of the first day after transplantation is probably much higher than the cost of the last day in hospital, due to much higher resource use. In a similar fashion, the impact of changes in other variables could be explored. If the cost of diagnostic testing was reduced by 50%, the total cost could be reduced by 6.7%. A 50% reduction in medication costs would reduce overall costs by 3.8%.

Estimation of additional costs

In preparation for the transplant-costing project of the Joint Policy and Planning Committee,[13] Toronto General Hospital estimated the costs of pre-transplantation care based on actual program data. The cost of nursing, diagnostic tests, administration and professional services was estimated to be Can$8059 in 1998 (S. McIntaggart, Multiple Organ Transplant Unit, Toronto General Hospital: Unpublished data, 1998). For 1991 and 1992, a total of Can$400 733 would have been spent on house-staff salaries for the liver transplant service.[14] If this sum is allocated equally to all 121 patients, Can$3312 is added to the cost of each transplant. The cost of outpatient follow-up care, including coordination, medical day unit costs, support staff and bloodwork was estimated to be Can$9800 for the first 12 months in 1998 (S. McIntaggart: Unpublished data, 1998). Assuming that follow-up for the second year would cost two-thirds of the amount for the first year, total follow-up cost was Can$16 333.

Assuming a discount rate of 5% and that all follow-up costs were incurred at the end of 1991, the total measured mean cost of the post-transplantation phase is reduced from Can$13 419 to Can$12 577. This changes the overall transplant cost from Can$89 066 to Can$88 225. The estimated outpatient follow-up costs that occur in the 2 years after transplantation, can be similarly discounted, resulting in an approximation of the follow-up costs of Can$15 259.

Fig. 1 shows a summary of all costs involved in liver transplantation, including the mean of those captured in the present analysis, plus those estimated from other sources. All of these values have been discounted and adjusted for inflation.

Table 4

Bivariate Relationship Between Predictor Variables and High Cost (*p* Value)

Variable	Pre-transplantation	Transplantation	Post-transplantation	Overall
Age in decades	0.7067	0.9814	0.5575	0.8265
Sex	0.2879	1.0000	0.7592	0.7592
Patient status 3 or 4*	0.2239	0.0292	0.6605	0.0017
Diagnosis	0.7366	0.3114	0.6627	0.4042
Survival	0.1824	0.3648	0.0977	0.4225
Cytomegalovirus infection	0.1060	0.6368	0.0001	0.0041
Severe rejection	0.2529	0.5354	0.0726	0.0204
Additional operation	0.4923	0.0175	0.3162	0.0071
Biliary complications	0.9702	0.0079	0.2778	0.1249

*Severity of liver disease: status 3 = intensive care unit, status 4 = fulminant.

Table 5

Logistic Regression Models Predicting High Cost of the Transplantation Phase

Variable	Odds ratio	95% confidence interval	*p* value
Transplantation phase			
Status 3–4 v. status 1–2*	4.40	1.28–15.10	0.0184
Additional operating room required	3.36	1.31–8.62	0.0116
Biliary complications	7.71	2.00–29.66	0.0030
Post-transplantation phase			
Cytomegalovirus infection	6.62	2.46–17.79	0.0002
Overall cost			
Status 2 v. 1	4.33	1.61–11.64	0.0037
3–4 v. 1	11.97	2.67–53.67	0.0012
Cytomegalovirus infection	6.12	2.04–18.39	0.0012
Additional operation	4.22	1.48–12.04	0.0070
Biliary complications	5.00	1.23–20.27	0.0242

*Severity of liver disease: status 1 = at home, status 2 = in hospital, status 3 = in intensive care unit, status 4 = fulminant.

Discussion

The affordability of organ transplantation has been questioned.[1] Transplant programs consume considerable resources and many costs are difficult to quantify, since they are often subsumed in the general running expenses of the hospital. As early as 1986, it was widely accepted that kidney transplantation had been proven to be cost-effective when compared with dialysis.[18] For other organ transplants, including heart,

lung and liver, there is often no alternative to transplantation other than death, which is likely to be considerably less costly to third-party payers.[18] However, death may not be less expensive when all costs to the family and society as a whole are taken into account. In conditions such as primary biliary cirrhosis, which often leads to liver failure in young women in their most productive years, liver transplantation has resulted in up to 94% returning to the work force full-time or part-time.[8]

In the present analysis, the estimated total cost of liver transplantation in 1998 from the date of listing to the second anniversary of the transplantation was found to be Can$121 732, from the perspective of the Government of Ontario.

Very little data are available on the costs of liver transplantation in Canada. In Ontario, the Joint Policy and Planning Committee created a Transplantation Working Group, which prepared a report on transplant costing.[13] The mean direct cost of liver transplantation in 1998 was estimated to be Can$85 749, not including organ procurement. The Committee's analysis estimated a total cost Can$36 000 less than the present analysis. There are several reasons for the discrepancy in estimated total cost. The Committee did not include professional fees, organ transportation costs or hospital overhead costs. In addition, the Committee assumed a total hospital stay of 16 days, compared to the measured mean value of 43 days in the present analysis. Also, the Joint Policy and Planning Committee's project did not specifically track individual patients, making comparisons of costs among groups of patients impossible.

A study from The Netherlands appears to have been the first attempt at rigorous cost analysis of liver transplantation.[19] The total cost in 1987 from the pre-transplantation phase to the end of the second year of follow-up was US$105 104. A second Dutch study analyzed costs for 152 liver transplantations performed between 1979 and 1990.[20] The costs for patients with biliary cirrhosis were estimated at approximately US$131 500, including costs incurred during 10 years of follow-up. Evans and associates[6] examined the issues involved in the economics of liver transplantation in the United States. They outlined a number of costing estimates. The Department of Health and Hu-

Table 6

Estimated Total Cost of Liver Transplantation

Cost	1998 $Can
Mean measured total transplantation cost (post-transplantation discounted @ 0.05 pa)	94 853
Estimated transplantation work-up cost	8 059
Estimated housestaff cost	3 561
Estimated follow-up cost (follow-up discounted @ 0.05 pa)	15 259
Total liver transplantation costs, Including estimates of work-up, housestaff and follow-up	121 732

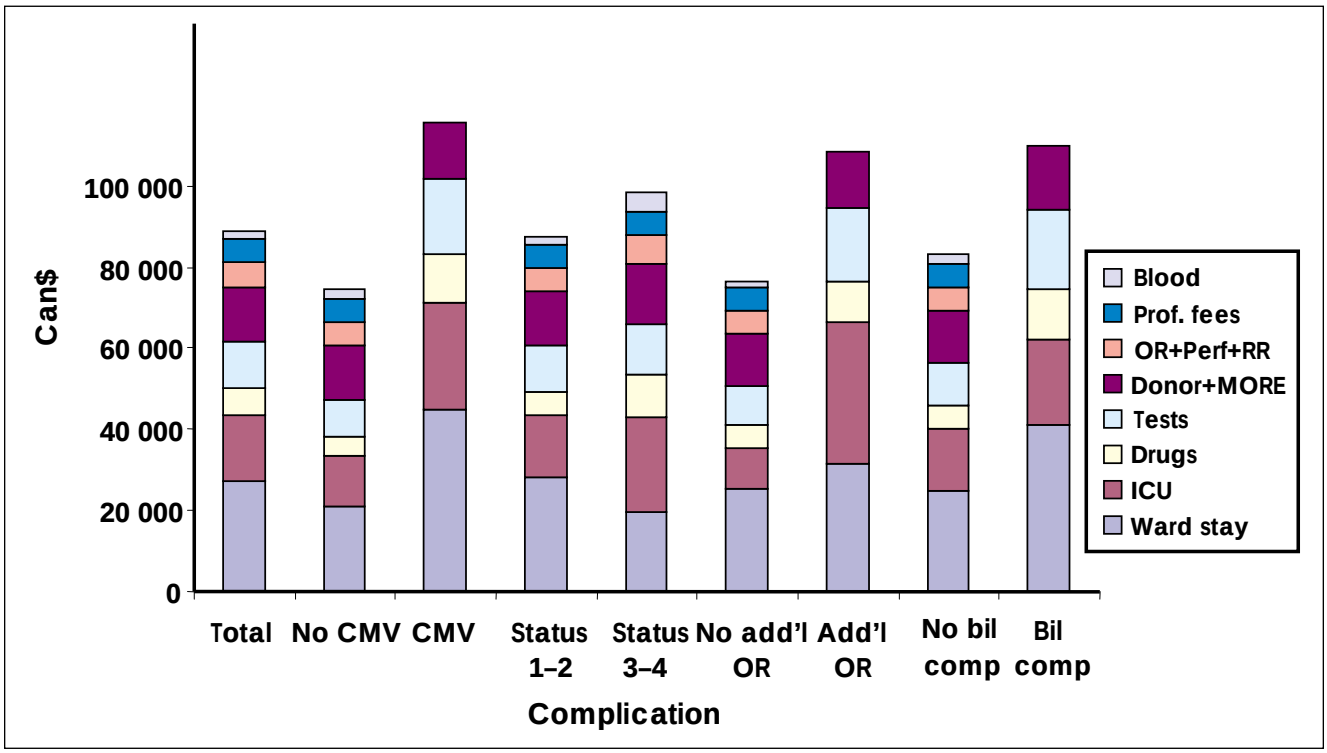

FIG. 1. Contribution of elements to total cost by complication (in Canadian dollars). CMV = cytomegalovirus, OR = operating room, bil comp = biliary complications, Prof. = Professional, Perf = perfusionist, RR = recovery room, MORE = Multiple Organ Retrieval and Exchange, ICU = intensive care unit.

man Services estimated first-year costs of US$240 000 in 1983, whereas an earlier review in Massachusetts placed the average total first year cost at US$230 000. Blue Cross and Blue Shield of Massachusetts estimated liver transplantation costs at US$270 000, assuming a postoperative stay of 61 days. Evans and associates[6] analyzed data collected in conjunction with the US National Cooperative Transplantation Study on 1680 liver transplants performed in 74 US centres in 1988. The median procedure charges totalled US$145 795.30. Most of the published studies on liver transplant costs have been incomplete analyses from the US that used charge data in place of true costs.[7] A major problem with using charge data is that charges may bear little relationship to costs and may vary greatly across hospitals. Charges are set by hospitals based on factors such as estimated costs, market conditions, payer mix and revenue maximization strategies.

In the present analysis, the factors associated with high cost of liver transplantation were severe liver disease, post-transplantation CMV infection, additional operative procedures and biliary complications. Investigators from the Mayo Clinic have studied preoperative predictors of increased resource utilization in liver transplantation.[9] They concluded that a Karnofsky score of 40 or less, poor nutritional status and renal failure independently predicted increased utilization.[9] Evans and associates[6] found that increased cost was associated with age under 50 years, nonwhite racial status, repeat transplantation, intensive care unit admission before transplantation and death at less than 1 year after transplantation.[13] Pageaux and colleagues[21] found that in France the first-year hospital costs of liver transplantation for alcoholics averaged US$86 000, compared with US$63 000 in nonalcoholics. Whiting and colleagues[22] from Ohio studied the influence of clinical variables on hospital costs after liver transplantation. Multivariate analysis demonstrated that length of stay, repeat transplantation and postoperative dialysis were independently associated with increased costs. A more recent analysis at 3 US centres found that recipients who were over 60 years of age, had liver disease due to alcohol abuse or were severely ill were the most expensive to treat.[23]

A multihospital study from Boston explored the impact of a series of variables on the costs of liver transplantation in the first year postoperatively, including costs of the admission for transplantation.[24] In a multivariate analysis, bacteremia, CMV disease, abdominal reexploration, age under 16 years and the number of units of blood products tranfused were found to be independently associated with longer post-transplantation hospital stay. The median cost for the first year after transplantation was US1994$66 665. The impact of CMV infection on current costs may be diminished owing to prophylactic drug regimens used by transplant programs. The patients at highest risk are seronegative recipients receiving livers from seropositive donors, and many centres currently routinely treat these patients with antiviral agents.[25,26]

Some authors have reported a decrease in costs over time. One American group reported that the hospital charges declined from an average of US$154 000 for the period 1991–1992 to US$103 000 for the period 1993–1995.[27] Another US group found that hospital charges in constant 1985 US dollars declined from a median of $71 922 in the period 1985–1986 to $49 970 in the period 1995–1996.[28]

The cost of a health intervention cannot be considered in isolation. The costs of alternative interventions must be considered, because they always entail costs. The only alternative to liver transplantation in most cases is deterioration and death. The costs associated with the treatment of ESLD have not been rigorously established. A group in Tennessee examined the charges for patients who would have met candidacy requirements for liver transplantation but died without receiving a transplant.[29] The mean hospital charge for 20 of these patients during the last 12 months of their lives was US$45 643 in 1984, compared with US$92 866 for the first year after liver transplantation. The hospital costs associated with the medical management of the last year of life for alcoholics with cirrhosis was found by another group to be US$31 000 in 1993.[22] The cost of dying of ESLD in Hawaii has been examined.[30] One hundred and fifty-three patients treated between 1991 and 1995 were studied with respect to mean inpatient hospital charges and length of hospital stay. The mean charge for 129 patients admitted with esophageal varices was US$30 980. Seven patients admitted to the liver team died of ESLD, with a mean charge of US$110 576. Transjugular intrahepatic portosystemic shunts were performed in 17 patients with a mean charge of US$43 209. Surgical shunts were undertaken in 6 patients with a mean charge of US$53 994. Seven patients received liver transplants at a mean charge of US$222 968.

Retrospective economic analyses have serious shortcomings. Care delivered in the past may not be representative of care delivered in the future.[31] This is particularly true of transplantation, in which dramatic changes may occur over a short period. Also, changes in overall patterns of health care delivery have reduced hospital stays for many surgical procedures.[32] The current analysis was based on patients treated in 1991 and 1992, in which the mean intensive care unit stay was 9 days and the mean ward stay was 34 days. For the data submitted to the Joint Policy and Planning Committee, Toronto General Hospital assumed an intensive care unit stay of 4 days and a ward stay of 12 days. This appears to have been based on a small

number of analyzed cases, and may not be representative of current mean values.

In Canada, liver transplantation is performed in 5 teaching centres. The other Canadian programs appear to have a similar mix of indications for transplantation to those in Toronto.[5] Costs of organ retrieval should be comparable throughout Canada, but medical fees vary considerably. It is difficult to predict whether these findings are generalizable to US centres. The indications for transplantation are very similar to the Canadian experience,[27,28,33,34] but the severity of disease is difficult to assess from the published data. Differences in practices may result in significant variations in overall costs.

Summary and conclusions

From the perspective of the Government of Ontario, the cost of liver transplantation from the date of placement on the waiting list to the end of the second year of follow-up was studied. The overall mean measured cost of liver transplantation was found to be Can$89 066 (range from $30 505–$690 431). When estimates of non-measured costs were included, appropriate discounting for follow-up costs carried out, and adjustments made for inflation, the cost in 1998 Canadian dollars was $121 732.

Multivariate logistic regression models were developed for costs of each phase and for overall costs. For the overall measured cost of liver transplantation, the variables associated with high cost were, in-hospital status before transplantation (odds ratio = 11.97), CMV infection (odds ratio = 6.12), additional operative procedure (odds ratio = 4.22) and biliary complications (odds ratio = 5.00). For all variables, the element that contributed the most to the high cost was in-hospital stay.

To reduce the cost of liver transplantation, a strategy of doing the procedure earlier in the course of the disease should be considered. The elimination of CMV infection and the reduction of biliary complications may also be desirable. Shortening the length of hospital stay after transplantation may be an effective strategy to reduce overall costs.

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SESAP Question
Question SESAP

Category 13, Item 1

Which of the following statements about endoscopic ultrasound study (EUS) for the staging of gastrointestinal cancers is NOT true?

(A) EUS is superior to computed tomography (CT) in detecting T N stage of esophageal tumors
(B) Enlarged celiac nodes can be detected and biopsied by EUS
(C) The sensitivity of EUS for detecting pancreatic malignancies is greater than 90%
(D) EUS characteristics of benign inflammatory lesions differ from those of malignant lesions
(E) EUS is more sensitive and specific than CT for staging of pancreatic tumors

For the answer and a critique of item 1 see page 466.