

SPECIAL ARTICLE

THE COST EFFECTIVENESS OF PREOPERATIVE AUTOLOGOUS BLOOD DONATIONS

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Abstract Background. Since the recognition that human immunodeficiency virus is transmissible by blood transfusion there has been increasing public and professional support for autologous blood donations before elective surgery. Autologous blood donation is, however, a more expensive process than the donation of allogeneic blood by community volunteers. Furthermore, there have been recent improvements in the safety of the volunteer blood supply.

Methods. We used a decision-analysis model to assess the cost effectiveness of donating autologous blood for four surgical procedures. Cost data were collected from the observation of transfusion practice at the University of California, Los Angeles, in 1992. Estimates of the risks of transfusion-associated diseases and the costs of treating them came from the medical literature. Cost effectiveness was expressed in dollars per quality-adjusted

year of life saved. We performed sensitivity analyses of the variables in our model and examined the effect of strategies suggested to reduce costs.

Results. Substituting autologous for allogeneic blood resulted in little expected health benefit (0.0002 to 0.00044 quality-adjusted year of life saved) at considerable additional cost (\$68 to \$4,783 per unit of blood). The additional cost of autologous blood was primarily a function of the discarding of units that were donated but not transfused and of a more labor-intensive donation process. The cost-effectiveness values ranged from \$235,000 to over \$23 million per quality-adjusted year of life saved.

Conclusions. Given the improved safety of allogeneic transfusions today, the increased protection afforded by donating autologous blood is limited and may not justify the increased cost. (N Engl J Med 1995;332:719-24.)

THE epidemic of the acquired immunodeficiency syndrome (AIDS) has increased concern about the risk of transmitting infectious diseases through blood transfusion. In response to this concern, there has been a dramatic increase in preoperative autologous blood donations over the past decade.¹⁻⁴ Although sensationalized reports of the dangers of blood transfusion continue in the lay press,⁵ there have been great improvements in the safety of the blood supply, primarily because of rigorous donor screening and sensitive serologic tests for the human immunodeficiency virus (HIV) and for hepatitis C virus.⁶

Autologous blood is more costly than allogeneic blood. Its donation entails greater administrative expense and a longer, more labor-intensive process of collection. Moreover, the frequency of positive tests for infectious disease in autologous units^{7,8} has raised questions about the safety of transfusing unused autologous units into patients other than the donor. Because of this concern, 85 percent of U.S. blood centers do not retain unused autologous units for other patients, but rather destroy them.⁹ This practice has substantially raised the cost of autologous transfusion.

The current national debate on health care reform

makes this an appropriate time to analyze the cost effectiveness of autologous blood donation. In our study, we determined the costs of providing patients with autologous blood and used decision-analysis techniques to calculate the cost effectiveness of substituting autologous for allogeneic blood. We also analyzed the value of various strategies to minimize the costs of autologous-donation programs.

METHODS

Calculation of Cost Effectiveness

We defined the incremental cost effectiveness of the use of autologous blood as the net change in the amount of health care resources required to collect and transfuse an autologous unit, instead of an allogeneic unit, divided by the net change in the amount of health benefits resulting from this substitution. A higher cost-effectiveness value thus defined represents a lower degree of cost effectiveness.

Costs were assessed from a social perspective and were considered to reflect only the expenditure of health care resources, not indirect expenses such as wages or productivity lost because of illness or death. Effectiveness was expressed in quality-adjusted years of life saved by the avoidance of transfusion-associated infectious disease.

Because some of the costs and benefits in our model were assumed to occur in the future, we discounted their future value at a rate of 5 percent per year to estimate present value.^{10,11} We used Excel spreadsheet software (Excel 4.0, Microsoft, Redmond, Wash.) to calculate cost effectiveness.

Data on Transfusion

We analyzed transfusion patterns in four procedures. Two procedures had high probabilities of requiring transfusion (total hip replacement and coronary-artery bypass grafting), and two had low transfusion probabilities (abdominal hysterectomy and transurethral prostatectomy). We reviewed the transfusion records of all patients undergoing these procedures at the University of California, Los Angeles (UCLA), Medical Center in 1992 for each patient's age and sex, the number of autologous units deposited, and the number of units transfused (Table 1). We also collected data on the discarding of al-

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logeneic blood due to factors such as positive tests or markers for infectious disease, units being outdated, and acute transfusion reactions.

Cost Variables

Direct Costs

We studied the blood-donation process for donors of both types of blood to determine the resources required for the recruitment, screening, and interviewing of donors; administrative record-keeping; and phlebotomy. To estimate other direct costs we relied on a survey conducted by the UCLA Division of Management Sciences that examined the actual costs to the university's blood center of infectious-disease and compatibility testing, blood processing, and inventory management. On the basis of these studies, we estimate that the average direct costs of autologous and allogeneic units at UCLA in 1992 were \$198.04 and \$149.80, respectively — a difference of \$48.24 per unit. A breakdown of these cost estimates is shown in Table 2.

Cost of Discarded Units

In order that the cost of discarded units be reflected in the average cost of a unit transfused, we divided the direct cost per unit by the rate at which units collected were actually transfused. For example, dividing the direct cost of an autologous unit, \$198 (Table 2), by the rate of units used in hip surgery, 0.84 (Table 1), yielded \$236 as the cost of a transfused autologous unit for that procedure. Repeating these calculations for the other procedures studied resulted in per-unit costs of \$275 for coronary-artery bypass grafting, \$762 for hysterectomy, and \$4,951 for transurethral prostatectomy.

The discarding of units was also a factor in determining the total cost of a transfused unit of allogeneic blood. We calculated that the cost of discarded units added another \$9.72 to the average cost of each unit transfused. We also added \$3.87 to represent the cost of cross-matching units of allogeneic blood that were not transfused into their initially intended recipients. This brought the total indirect cost of unused blood to \$13.59 per unit transfused.

Costs of Treating Complications of Transfusion

For each of several viruses transmissible by transfusion, we estimated the per-unit probability of infection in donated allogeneic blood (Table 3). We also estimated the per-unit probability that patients receiving transfusions of infected blood would have each of the forms of disease associated with the given virus (Table 3). We then multiplied these two per-unit probabilities by the estimated costs of treating each disease.

We discounted the costs of treating patients with transfusion-associated hepatitis on the basis of a median life expectancy of 18 years.¹² Using this technique we estimated that the lifetime cost of treating transfusion-associated hepatitis¹³ added \$4.05 to the cost of each allogeneic blood unit. Similarly, the cost of treating HIV infection added another \$0.63 per allogeneic unit, on the basis of an estimated lifetime treatment cost of \$119,000,¹⁴ multiplied by our base-line estimate of the per-unit risk of HIV (Table 3) and discounted over nine years of expected survival.

We were unable to find estimates of the cost of treating diseases

Table 2. Direct Costs of Collecting, Testing, and Processing Autologous and Allogeneic Blood.

ITEM	COST PER UNIT (\$)	
	AUTOLOGOUS	ALLOGENEIC
Collection		
Labor	87.66	43.15
Equipment	41.76	41.76
Infectious-disease testing*		
Initial	23.58	23.58
Confirming	0.69	0.09
Blood processing and inventory management		
Labor	26.94	23.83
Equipment	1.22	1.20
Compatibility testing		
Labor	15.00	15.00
Equipment	1.19	1.19
Total	198.04	149.80

*Blood was tested for syphilis, hepatitis B surface antigen, antibodies to hepatitis B core antigen, antibodies to hepatitis C virus, antibodies to HIV types 1 and 2, and antibodies to HTLV-I and HTLV-II; alanine aminotransferase was also measured.

caused by human T-cell lymphotropic virus types I and II (HTLV-I and HTLV-II). However, even if we assumed that these costs were as high as those incurred for treating HIV infection, they would add only about five cents per unit, because the probability that these complications will develop is so low (Table 3). We did not model the costs of other transfusion-acquired infectious diseases because of their extreme rarity in the United States.⁶

On the basis of practice at UCLA, we estimated that the average cost of diagnosing an acute transfusion reaction added seven cents per unit in undiscounted costs. Delayed hemolytic transfusion reactions were excluded from consideration because they are unusual and rarely cause serious morbidity.¹⁵ Costs of treating acute hemolytic transfusion reactions were also excluded, since these happen most commonly when a unit of blood is transfused into the wrong patient.^{15,16} The risk of this type of human error is independent of the category of blood donation.

We chose not to model the possible immunomodulating effects of allogeneic transfusion.¹⁷⁻²² The current evidence of these effects comes primarily from retrospective studies, and not all investigators agree that a causal link has been established.²³⁻²⁵

Taken together, transfusion-related complications added \$4.80 to the cost of each unit of blood. Adding this indirect cost, the \$13.59 indirect cost of unused blood, and the direct cost of \$149.80 yielded a total cost of transfused allogeneic blood of \$168.19 per unit.

Effectiveness Variables

We used published estimates of the probabilities, per unit of blood, of contracting transfusion-associated infections and of the likelihood of various disease outcomes resulting from those infections. The values assigned to the effectiveness variables in our model were based, whenever possible, on the best estimates available, but when assumptions or estimates were equivocal, we assigned values that tended to bias our results in favor of autologous donation.

For example, in our base-line analysis we used 0.0003 and 0.000005 as the risks of transmission of hepatitis C virus²⁶ and of hepatitis B virus,⁶ respectively, along with the estimates of the probability of various outcomes^{13,27} presented in Table 3. In the largest prospective study to date of transfusion-related hepatitis, however, mortality from all causes after an average follow-up of 18 years was the same (51 percent) for transfusion recipients in whom hepatitis developed as for a matched group of transfusion recipients in

Table 1. Transfusion Data on Patients Donating Autologous Blood for Four Surgical Procedures.

PROCEDURE	NO. OF PATIENTS	AGE (YR)	SEX (M/F)	UNITS TRANSFUSED	UNITS DONATED	UNITS TRANSFUSED/ UNITS DONATED
Total hip replacement	80	62 (23-83)	32/48	191	228	0.84
Coronary-artery bypass grafting	24	67 (50-84)	23/1	36	50	0.72
Abdominal hysterectomy	16	49 (26-70)	0/16	5	19	0.26
Transurethral prostatectomy	21	68 (44-77)	21/0	1	25	0.04

Table 3. Estimates Used in the Base-Line Calculations.

VARIABLE	ESTIMATE
Probability of infection (per allogeneic unit)	
Hepatitis C virus	0.0003
Hepatitis B virus	0.000005
HIV	0.0000067
HTLV-I and HTLV-II	0.000017
Probability of disease*	
Hepatitis C virus	
Persistent hepatitis	0.28
Active hepatitis	0.13
Cirrhosis	0.10
Fulminant hepatitis	0.01
Hepatitis B virus	
Carrier status	0.04
Persistent hepatitis	0.02
Active hepatitis	0.01
Cirrhosis or cancer	0.01
HIV	
AIDS	1.0
HTLV-I and HTLV-II	
ATL or HAM†	0.04
Quality adjustments for various health states	
Persistent hepatitis	0.99
Active hepatitis	0.90
Cirrhosis or cancer	0.90
Fulminant hepatitis	0
HIV infection	0.75
AIDS	0.50
ATL or HAM†	0.90

*Per unit of infected blood transfused.

†ATL denotes adult T-cell lymphoma, and HAM HTLV-associated myelopathy.

whom hepatitis did not develop.¹³ Despite this finding, we made the assumption — in favor of autologous donations — that there is excess mortality of 0.9 percent per year among transfusion recipients who contract hepatitis. We assumed that all those in whom fulminant hepatitis develops die immediately after transfusion.

Recent estimates of the risk of infection with HIV are as low as 1 infected unit per 225,000.⁶ We used a higher estimate of 1 unit per 150,000 (0.0000067).²⁸ Our undiscounted estimates of the average latency period from the time of infection with HIV to the development of AIDS²⁹ and the mean survival time after the diagnosis of AIDS are seven and two years, respectively.

The risk of transmission of HTLV-I or HTLV-II through allogeneic transfusion is currently estimated to be 1 infected unit per 60,000 (0.000017), with a maximally estimated 4 percent lifetime risk that clinically active disease will develop in patients who become infected.^{30,31}

Base-line life expectancies were obtained from U.S. vital-statistics life-table data³² and discounted at a rate of 5 percent per year. The effect of transfusion complications on discounted life expectancies was calculated with use of the 0.75 Mixed Declining Exponential Approximation of Life Expectancy.³³

We adjusted our life-expectancy calculations to reflect the relative desirability of various states of health associated with possible complications of allogeneic transfusion. We then expressed the outcomes in quality-adjusted years of life. The values assigned to specific health states in our analysis (Table 3) represented our consensus after reviewing the relevant medical literature.³⁴⁻³⁷

Sensitivity Analysis

The variables in our decision-analysis model were analyzed over a range of values in a process known as sensitivity analysis. This was done to determine the stability of

our results and to gauge the effects of uncertainty in the values we assigned to these variables. We also analyzed the potential effect of some suggestions to lower the cost of autologous-donation programs: reduced testing for blood compatibility and infectious disease,³⁸ the addition of unused units to the allogeneic blood supply,^{9,39} and the use of collection-schedule guidelines.⁴⁰ Finally, to demonstrate how our model might be generalized, we analyzed the cost effectiveness of autologous donation for hypothetical patients of various ages undergoing procedures with differing percentages of discarded units of blood.

RESULTS

The added cost of substituting an autologous unit for an allogeneic one ranged from \$68 to \$4,783 in the procedures we examined (Table 4). The higher cost of autologous blood, as well as its variation according to procedure, results mainly from the cost of discarded units. By comparison, the direct costs of producing an autologous unit, which we estimated to be \$48 higher than those for a unit of allogeneic blood, made a smaller contribution to the overall cost difference in three of the four procedures.

The incremental effectiveness of autologous blood was small in all four procedures, ranging from 0.0002 to 0.00044 quality-adjusted year of life (about two to four hours) per unit (Table 4). The variation in effectiveness was a function of the different life expectancies of the average patients undergoing each procedure.

Finally, the incremental cost effectiveness, expressed as dollars per quality-adjusted year of life saved, varied from \$235,000 to over \$23 million (Table 4). Sensitivity analyses revealed that these results were not substantially altered by uncertainty in the values of any variable in the model. In fact, increasing the risk of contracting hepatitis C — the most sensitive risk variable in our model — by as much as 50 percent still resulted in a high cost-effectiveness value of \$167,000 per quality-adjusted year of life, even in hip surgery, the procedure we examined that was most likely to favor the use of autologous blood (Table 5).

Cost savings from reduced testing for blood compatibility and infectious diseases would have the most pronounced effects in hip surgery and coronary-artery bypass surgery, the procedures using the most transfused blood. Even for these, though, the resulting cost-effectiveness values were \$87,000 and \$263,000 per quality-adjusted year of life, respectively (Table 5).

Table 4. Base-Line Calculations of the Cost Effectiveness of Autologous Blood Donation in Four Surgical Procedures.

VARIABLE*	TOTAL HIP REPLACEMENT	CORONARY-ARTERY BYPASS GRAFTING	ABDOMINAL HYS-TERECTOMY	TRANSURETHRAL PROSTATECTOMY
Mean age of patient (yr)	62	67	49	68
Added cost per unit transfused (\$)†	68	107	594	4,783
Incremental effectiveness per unit transfused (QALY)†	0.00029	0.00022	0.00044	0.00020
Cost effectiveness (\$/QALY)	235,000	494,000	1,358,000	23,643,000

*QALY denotes quality-adjusted year of life.

†As compared with a unit of allogeneic blood.

Not surprisingly, saving unneeded autologous units for nondonor recipients would most improve cost effectiveness in the procedures in which autologous donations are least likely to be used by the donor. However, implementing such a policy would still result in cost-effectiveness values in the range of \$163,000 to over \$1 million per quality-adjusted year of life (Table 5).

Applying the principles of a "schedule of optimal preoperative collection of autologous blood," as described by Axelrod et al.,⁴⁰ would increase the amount of autologous blood collected and subsequently discarded, thereby dramatically elevating the cost-effectiveness values for most procedures. For example, donating five units would protect 90 percent of patients undergoing hip surgery from exposure to allogeneic blood, but would also result in the discard of 41 percent of the units and cost \$580,000 per quality-adjusted year of life saved (Table 5).

Table 6 demonstrates the effect on the cost effectiveness of autologous donation of the patient's age and the percentage of units discarded. Autologous donation is more cost effective for younger patients. However, even for the youngest patients undergoing procedures in which the percentage of discarded units is as low as

Table 6. Cost Effectiveness of Autologous Blood Donation, Assuming Various Rates of Use and Patient Ages.

AGE (YR)	PERCENTAGE OF UNITS TRANSFUSED				
	2%	25%	50%	75%	85%
	<i>cost effectiveness (\$/QALY)*</i>				
15	15,800,000	1,020,000	371,000	156,000	105,000
20	16,300,000	1,050,000	382,000	161,000	109,000
30	17,700,000	1,130,000	414,000	174,000	118,000
40	20,000,000	1,280,000	468,000	197,000	133,000
50	24,100,000	1,540,000	564,000	237,000	160,000
60	31,600,000	2,030,000	741,000	312,000	211,000
70	46,600,000	2,990,000	1,090,000	459,000	310,000

*QALY denotes quality-adjusted year of life.

15 percent, the cost-effectiveness value was at least \$105,000 per quality-adjusted year of life.

DISCUSSION

Discarded units are primarily responsible for the higher cost of autologous blood. The rates of use of blood units that we employed in our calculations were based on transfusion practice during one year at one institution. Such rates can change over time and vary from one institution to another, but we do not believe that the highest rate of use we found, 0.84, could be substantially improved. Because of the wide variation in the transfusion requirements of patients undergoing hip-replacement surgery — from 0 to 12 units — 16 percent of autologous units were discarded in that procedure, despite the fact that the mean donation (3 units) was equal to the mean number of units transfused.

The greater direct costs associated with the use of autologous units also made an important contribution to the unfavorable cost-effectiveness values that we found. A more labor-intensive donation process is primarily responsible for these higher costs. The scheduling of autologous donation requires the time of administrative personnel and physicians to coordinate donations with individual surgical schedules. Despite the abbreviated medical-history questionnaire used for autologous donors, their screening interviews take longer because autologous donors tend to have more involved medical histories than allogeneic donors. Potential autologous donors are also more likely to be asked to

Table 5. Cost Effectiveness of Autologous Blood Donation in Four Surgical Procedures under Various Assumptions.

ASSUMPTION	TOTAL HIP REPLACEMENT	CORONARY-ARTERY BYPASS GRAFTING	ABDOMINAL HYSTERECTOMY	TRANSURETHRAL PROSTATECTOMY
	<i>cost effectiveness (\$/QALY)*</i>			
Base line	235,000	494,000	1,358,000	23,643,000
Risk of HCV increased 50% over base-line estimate†	167,000	350,000	959,000	16,750,000
Risk of HIV increased 50% over base-line estimate	218,000	455,000	1,258,000	21,768,000
Difference in direct costs reduced 50%‡	135,000	337,000	1,147,000	20,662,000
Quality of life decreased 50% from base-line estimate	200,000	410,000	1,190,000	19,492,000
Discount rate reduced from 5% to 2.5%	171,000	387,000	870,000	18,951,000
Minimal compatibility testing (ABO, Rh), saving \$12 per unit	184,000	416,000	1,252,000	22,160,000
Elimination of infectious-disease testing, saving \$24 per unit	135,000	342,000	1,147,000	20,677,000
Minimal compatibility testing and elimination of infectious-disease testing, saving \$36 per unit	87,000	263,000	1,041,000	19,194,000
50% of unused units added to allogeneic blood supply	163,000	287,000	334,000	1,053,000
Schedule of optimal collection§	580,000	1,190,000	1,427,000	No collection

*QALY denotes quality-adjusted year of life.

†HCV denotes hepatitis C virus.

‡As compared with allogeneic blood donation.

§The schedule of optimal preoperative collection of autologous blood described by Axelrod et al.⁴⁰ recommends the donation of enough autologous units to ensure that 90 percent of patients avoid allogeneic transfusion. Given the transfusion practice at UCLA in 1992, five units would have been necessary for hip replacement, six units for bypass grafting, one unit for hysterectomy, and no units for prostatectomy.

defer donation. They thus require more counseling about the reasons for deferral (e.g., intercurrent illness or low hematocrit) and the alternatives open to them. Finally, phlebotomy is a longer process for autologous donors, who tend to be older and more frail than allogeneic donors.

Labor-related direct costs may be greater at UCLA than at other institutions, but even when we halved our base-line estimate of the additional direct costs of autologous blood, the cost-effectiveness values were never lower than \$135,000 per quality-adjusted year of life (Table 5).

Previous analyses of the cost effectiveness of autologous blood donation for hip surgery⁴¹ and coronary-artery bypass grafting⁴² used decision-analysis techniques similar to ours. Although this earlier work used estimates of direct costs based on Medicare cost-to-charge ratios, it produced results consistent with our own. These studies have been criticized for using hospital charge data to estimate true costs,³⁸ but their results support our conclusion that autologous blood donation is not as cost effective as many of its proponents believe.

Some transfusion-medicine specialists have suggested strategies to make this medical service more cost effective.^{9,38-40} We found that reducing testing for blood compatibility and the presence of infectious disease might substantially improve cost effectiveness. However, this strategy reduced the cost-effectiveness value to less than \$100,000 per quality-adjusted year of life in only one procedure (Table 5). Furthermore, the actual cost savings from reduced testing would be limited to hospital-based blood centers, which collect only half the nation's autologous blood.⁴ Exemptions from Food and Drug Administration testing requirements are possible only for units of autologous blood donated and transfused at the same institution.

The rather small effects of adding unused autologous units to the allogeneic blood supply (Table 5) may seem especially surprising, given our finding that their destruction is the most important reason for the higher cost of autologous blood. However, because donors of autologous blood tend to have more medical problems than community volunteer donors, we estimated that only half these units would meet the strict requirements for infectious-disease testing and history taking that apply to allogeneic donation.

We may have actually overestimated the improvement in cost effectiveness resulting from the use of autologous blood for nondonor patients. Others have estimated that only 30 percent of these units would be suitable.³ Moreover, we did not model the increased administrative costs that could be expected for labeling and maintaining two separate autologous-blood inventories (one eligible and one ineligible for use with other patients).

The perception and assessment of risk by the public, as well as by medical professionals, is a complex proc-

ess. It is probably greatly influenced by media coverage that often focuses on the most negative and dramatic examples of complications of medical practices and procedures.⁵ Studies, such as ours, that attempt to quantify the risks and benefits of blood transfusion could well be used as a starting point for more informed discussions between doctors and patients.

Our decision-analysis model could also be used to develop guidelines for more responsible use of this expensive medical practice. Some previous guidelines for autologous blood donation require only that a patient's hemoglobin be above a certain level.^{2,43} Others recommend donation from patients with at least a 10 percent probability of requiring transfusion.^{9,44} But these criteria promote donation in circumstances in which many units would be destroyed and where, according to our study, the cost per quality-adjusted year of life saved could be as high as several million dollars (Table 6).

Our estimates of cost effectiveness reflect a social perspective, but they also have an economic impact at the institutional level. Under current Medicare reimbursement policies, discarded autologous blood units increase a hospital's unreimbursed expenses for performing surgery on Medicare patients.⁴⁵

Individual patients, anxious about the risks of allogeneic transfusions, may be willing to pay the added costs of autologous donation themselves. Whether society should be willing to pay to relieve this anxiety has yet to be resolved, despite those who challenge the insurance industry and the federal government to "recognize their responsibility to pay reasonable charges for the valuable service of autologous blood collection."⁴⁰

Although there is no currently accepted absolute standard by which the effectiveness of a medical intervention can be judged to be worth its cost, our analysis represents one method to assess various uses of limited health care resources. Society should consider whether its interests are best served by paying for autologous blood donations when other practices, already proved to be much more cost effective, have not yet been made universally available.

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