Cost Analysis of Hematopoietic Stem Cell Transplantation in Adult Patients with Acute Myeloid Leukemia at King Chulalongkorn Memorial Hospital

Sureerat Ngamkiatphaisan MSc*, Jiruth Sriratanaban MD, PhD**,
Pirom Kamolratanakul MD, MSc***, Tanin Intragumtornchai MD, MSc***,
Nopadon Noppakun MD**, Pongpisut Jongudomsuk MD****

** Health Insurance Coordinating Center, King Chulalongkorn Memorial Hospital, Bangkok*
*** Faculty of Medicine, Chulalongkorn University, Bangkok*
**** Faculty of Medicine, Chulalongkorn University, Bangkok*
***** Bureau of Policy and Planning, National Health Security Office, Bangkok*

The purpose of the study was to analyze the first-year cost of hematopoietic stem cell transplantation (HSCT) program for the treatment of adult patients with acute myeloid leukemia (AML) at King Chulalongkorn Memorial Hospital (KCMH). The present retrospective study was carried out on 67 AML patients treated with bone marrow transplantation (BMT) or peripheral blood stem cell transplantation (PBSCT) at KCMH during the period of 1994 to 2005. The actual total one-year cost from the provider perspective were determined by the reviewing medical records for medical care costs (MCCs) and by adjusting data from the reports of annual cost analysis of KCMH for routine services costs (RSCs). All costs were converted to 2006 values using the Thai consumer price indices. It was found that the full cost of allogeneic HSCT (allo-HSCT) and autologous HSCT (auto-HSCT) in the first year of the program was $22,592.85 and $24,171.25 per case respectively. Cost-effective appraisal, comparing with chemotherapy, need to be studied further.

Keywords: *Cost analysis, Hematopoietic stem cell transplantation, Acute myeloid leukemia*

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Hematopoietic Stem Cell Transplantation (HSCT) is one of the effective treatment options for Acute myeloid leukemia (AML). However, this treatment choice is a particular challenge due to problems in finding HLA-matched siblings and financial problems[1,2]. Particularly in Thailand there are only a few centers which are performing HSCT because of the multidisciplinary high-level support required. Nevertheless, the recent establishment of the National Health Security Scheme in this country in the year 2000 might provide better access for the Thai population to the treatment of AML. The treatments of hematological malignancies receive a special consideration, although the scheme generally reimburses the hospital costs for out-patient and in-patient services using capitation and DRG-based payments retrospectively. Since 2006 the fee schedule system called disease management program (DMP) has been the scheme paying for this disease group. Unfortunately, HSCT has been excluded from the protocols of treatment under this program.

For the HSCT had never been included in any preceding welfare programs for the general population and, thus, there were no supporting data. After one year of the disease management program, an evaluation team revised the treatment protocol and proposed HSCT for AML patients as a pilot project for the fiscal year of 2008.

DRG is a tool to group hospital costs based on medical and administrative data. The cost weights

Correspondence to : Ngamkiatphaisan S, Health Insurance Coordinating Center, King Chulalongkorn Memorial Hospital, Rama 4 Rd, Patumwan, Bangkok 10330, Thailand. Phone: 089-770-5477, 0-2256-4659, Fax: 0-2256-4112, E-mail: sureerat68 @gmail.com or trcsnk@md.chula.ac.th

express the relative cost for hospitalization, and are used, among other purposes, for reimbursement of hospital costs. The cost weight states the mean requirement of resources in each DRG group.

The Bureau of Policy and Planning of the National Health Security Office consequently asked for the evidence-based HSCT costing to prepare and allocate the budget for the revised hematological malignancy program. The total cost of HSCT has never been empirically explored in Thailand. As previous studies indicated the most of life-time cost of HSCT was first-year cost[1, 3]. The authors therefore studied the first-year cost of treating AML patients by HSCT at King Chulalongkorn Memorial Hospital (KCMH), one of the four teaching hospitals having capabilities to undertake the program. The findings eventually became a valuable input for the national scheme development.

Material and Method

Patients

The present retrospective study was carried out by using data collected from medical records. The presented included all medical records which summarized with international classification of disease and related health problem 10th revision (ICD-10) of C92.0, C92.4, C92.5, C93.0 and the patients' name were registered in the HSCT program of the division of Hematology, department of Medicine, KCMH during the period of 1994 to 2005. The AML patients having the ages over 60 were excluded. The presented found 67 AML patients treated with HSCT at KCMH. These patients' demographic data are shown in Table 1. Fifty-one patients were treated with allo-HSCT (PBSCT = 47, BMT = 4) and sixteen were treated with auto-HSCT (all were PBSCT). The ages of these AML patients were between 15 and 59 years. The mean age was 33.85 years (SD = 11.410).

Cost calculation

Applying the provider perspective, the first-year costs of the HSCT program per person consisted of MCCs and RSCs.

MCCs were summed from the cost of general drugs (all drugs except chemotherapeutic drugs), chemotherapeutic drugs, medical supplies, laboratory

Table 1. Demographic data of AML patients

Demographic data	Total		Allo-PBSCT		Auto-PBSCT	
	n	%	n	%	n	%
Age						
15-24	18	26.87	15	29.41	3	18.75
25-34	16	23.88	15	29.41	1	6.25
34-44	23	34.33	15	29.41	8	50.00
45-60	10	14.93	6	11.76	4	25.00
Career						
Unemployed / student	18	26.87	12	23.53	6	37.50
Employee	14	20.90	10	19.61	4	25.00
Civil servant	20	29.85	18	35.29	2	12.50
Private business	11	16.42	9	17.65	2	12.50
Others	4	5.97	2	3.92	2	12.50
Health insurance scheme						
UC scheme	10	14.93	6	11.76	4	25.00
CSMBS	32	47.76	26	50.98	6	37.50
SSS	8	11.94	8	15.69	0	0.00
Uninsured / cash	17	25.37	11	21.57	6	37.50
The French-American-British (FAB) Classification of Diseases						
M 1	1	1.49	1	1.96	0	0.00
M 2	24	35.82	17	33.33	7	43.75
M 3	1	1.49	1	1.96	0	0.00
M 4	21	31.34	15	29.41	6	37.50
M 5	9	13.43	8	15.69	1	6.25
M 6	2	2.99	1	1.96	1	6.25
Mixed	2	2.99	1	1.96	1	6.25
No information	7	10.45	7	13.73	0	0.00

tests, radiological investigations and radiation therapies, and blood or blood components.

Utilization reviews of medical records were used to collect the quantities of medical resources. The presented data used the secondary data of unit costs of laboratory tests, and radiological investigations and radiation therapies from KCMH research[4].

RSCs were adjusted data from the research and the reports of annual cost analysis of KCMH which included labor costs, material costs (except the costs of drugs, and medical supplies), capital costs and indirect costs allocating from all non-revenue producing cost centers and all revenue producing cost centers by simultaneous equations[4]. The presented data picked up the unit cost of RSCs in the clinic of hematology and relevant clinics (cost per visit) as well as the unit cost of RSCs in the wards of medicine and relevant wards (cost per patient-day). Then, these unit costs of RSCs were multiplied by number of visits for outpatients (OPs) and multiplied by length of stay (LOS) for in-patients (IPs).

The structure of the total cost is shown in Fig. 1. The cost calculation excluded the cost of donor preparation. All costs were collected in baht and were calculated in the 2006 values using the Thai consumer price indices[5-6]. The numbers were later converted into US dollars using the exchange rate of US$1 = 37.93 baht.

Treatment outcomes and one-year service utilization patterns of these patients were studied namely, LOS, number of OP visit, and number of hospitalization. All of these variables were collected by counting from OP and IP medical records. OP visits included OP services and day-care or ambulatory-care services.

Results

The outcomes of AML patients are demonstrated in Table 2, in terms of complete remission (CR) before HSCT was most achieved CR in 1 year follow-up (61.54%).

The total OP costs for allo-HSCT and auto-HSCT were $1,729.51 and $692.72 per case, respectively. The MCC and RSC of allo-HSCT were 72.77% and 27.23%, respectively. The MCC and RSC of auto-HSCT were 45.74% and 54.26%, respectively. The OP costs of allo-HSCT were higher than those of auto-HSCT, especially between 3rd and 4th month after HSCT. The OP costs of these period were $773 for allo-HSCT and $173 for auto-HSCT.

MCC of OP service of allo-HSCT was four-fold higher than auto-HSCT ($1,258.60 and $316.87 per case, respectively). Cost breakdown items in MCCs showed that general drugs were the foremost cost driver for allo-HSCT particularly in the 3rd-4th, 5th-6th, and 7th-8th month after allo-HSCT. These OP costs were $576, $467, and $293 per case per 2 months, respectively.

In the first two months of HSCT, MCC of IP service for auto-HSCT was lower than allo-HSCT. These were $9,105 and $10,226 per case, respectively. The peak of IP cost for auto-HSCT after harvesting was the general drug cost in the 7th-8th month that was $517 per case.

The total cost of auto-PBSCT was slightly higher than allo-PBSCT, $24,171 and $22,593 per case, respectively (Table 4). The primary cost driver of allo-PBSCT was the general drug cost (43.38%), followed by RSC (41.70%). The RSC and general drug costs being primary cost drivers of auto-PBSCT were 49% and 33.66%, respectively.

Discussion

The total costs of 51 AML patients treated with allo-HSCT and 16 AML patients treated with auto-HSCT in the first year of HSCT were $24,171.25 and $22,592.85 per case. Approximately 80% of the total costs incurred the first two months. The major

Table 2. One-year outcome of HSCT

Status at HSCT	One-year outcome							
	Total		Complete remission		Relapse		Death	
	n	%	n	%	n	%	n	%
Allogeneic HSCT in CR (n = 51)	37	100.00	22	59.46	5	13.51	10	27.03
Autologous HSCT in CR (n = 16)	15	100.00	10	66.67	0	0.00	5	33.33
Total in CR (n = 67)	52	100.00	32	61.54	5	9.62	15	28.85

CR = Complete remission

Table 3. Bi-monthly utilization of AML patients

Components	1st-2nd month		3rd-4th month		5th-6th month		7th-8th month		9th-10th month		11th-12th month		Yearly	
	Average per case	%	Average per case	%	Average per case	%	Average per case	%	Average per case	%	Average per case	%	Average per case	%
1) Allogeneic HSCT (n = 51)														
OP visit (time)	2.27	14.70	4.51	29.15	2.69	17.36	2.51	16.22	1.90	12.29	1.59	10.27	15.47	100.00
Amission time (time)	1.06	48.65	0.37	17.12	0.16	7.21	0.20	9.01	0.24	10.81	0.16	7.21	2.18	100.00
LOS (day)	40.45	75.29	6.16	11.46	1.55	2.88	2.57	4.78	1.73	3.21	1.27	2.37	53.73	100.00
2) Autologous HSCT (n = 16)														
OP visit (time)	1.44	11.06	3.63	27.88	3.31	25.48	1.94	14.90	1.19	9.13	1.50	11.54	13.00	100.00
Amission time (time)	1.25	60.61	0.13	6.06	0.19	9.09	0.25	12.12	0.06	3.03	0.19	9.09	2.06	100.00
LOS (day)	53.00	77.23	2.56	3.73	3.25	4.74	6.44	9.38	1.31	1.91	2.06	3.01	68.63	100.00

component of the cost was MCC, 58.3% in allo-HSCT and 51% in auto-HSCT. The major cost driver of allo-HSCT was general drug costs (43.38%) while the major driver of auto-HSCT cost was RSC (49%).

Total cost calculation for Thai health care services are difficult to establish, especially in tertiary care hospitals that have multiple departments and complicate functions. There were a lot of variations of financial and medical data among the large teaching hospitals capable to perform PBSCT. To avoid data variation, the authors confined the present study only at KCMH. This limitation made policy makers use these results only with reservations. Clinical and economic results from a medical-teaching center with a high level of experience in treating AML patients with PBSCT are lower than costs of centers with lower levels of experience[7]. As in the single-institution study, some conclusions are specific to the authors' center and reflect out specific mix of patients and practice patterns.

Most of the patients were civil servants (29.87%) that explained the amount of health insurance used for HSCT (47.76%). Only civil servants could receive HSCT. Moreover, some beneficiaries approved by the Medical Committee of the Social Security Scheme, also obtained HSCT. The remaining patients had to pay for medical expenses by themselves. The HSCT fund of KCMH therefore should support a number of low-income patients who are currently covered by the UC scheme.

Complete remission at HSCT was usually achieved CR within one-year follow-up (61.54%). This outcome of HSCT was consistent with other studies which found that first CR at HSCT was significantly better than the other status of patients at HSCT[8-10].

Data of utilization patterns (Table 3) show average LOS of auto-HSCT to be longer than allo-HSCT (68.63 compared to 53.73 days per case). This affected RSC of auto-HSCT to be higher than allo-HSCT and than the higher RSC, whereas, lower MCC of auto-HSCT affected total costs in the first year of auto-HSCT to be higher than allo-HSCT ($24,171.25 compared to $22,592.85 per case).

Although the authors endeavored to analyze the real costs of HSCT, the present study had to use data from annual cost analysis. Data in hospital budget and finance information are often included with routine hospital operating costs and are therefore very difficult to re-allocate to AML patients with HSCT.

MCC of OP in allo-HSCT was higher than auto-HSCT because of administration of immunosuppressant drugs such as cyclosporin in the 3rd-4th month

Table 4. The total first-year costs of HSCT

Components	Out-patients		In-patients		Total cost	
	Cost ($)	%	Cost ($)	%	Cost ($)	%
1) Allogeneic PBSCT (n = 51)						
1.1) MCC	1,258.60	72.77	11,913.10	57.10	13,171.69	58.30
General drugs	1,039.33	60.09	8,761.48	41.99	9,800.81	43.38
Chemotherapuetic medications	11.27	0.65	267.81	1.28	279.08	1.24
Medical supplies	6.84	0.40	222.01	1.06	228.85	1.01
Laboratory test	52.95	3.06	429.64	2.06	482.59	2.14
Radiological/radiation	15.47	0.89	455.27	2.18	470.74	2.08
Blood components	132.74	7.67	1,776.89	8.52	1,909.63	8.45
1.2) RSC	470.91	27.23	8,950.25	42.90	9,421.16	41.70
Total cost	1,729.51	100.00	20,863.35	100.00	22,592.85	100.00
2) Autologous PBSCT (n = 16)						
1.1) MCC	316.87	45.74	12,011.23	51.16	12,328.11	51.00
General drugs	127.88	18.46	8,007.53	34.11	8,135.41	33.66
Chemotherapuetic medications	1.58	0.23	361.84	1.54	363.42	1.50
Medical supplies	5.90	0.85	92.70	0.39	98.60	0.41
Laboratory test	16.38	2.36	217.76	0.93	234.14	0.97
Radiological/Radiation	9.77	1.41	443.60	1.89	453.37	1.88
Blood components	155.37	22.43	2,887.81	12.30	3,043.17	12.59
1.2) RSC	375.85	54.26	11,467.29	48.84	11,843.14	49.00
Total cost	692.72	100.00	23,478.53	100.00	24,171.25	100.00

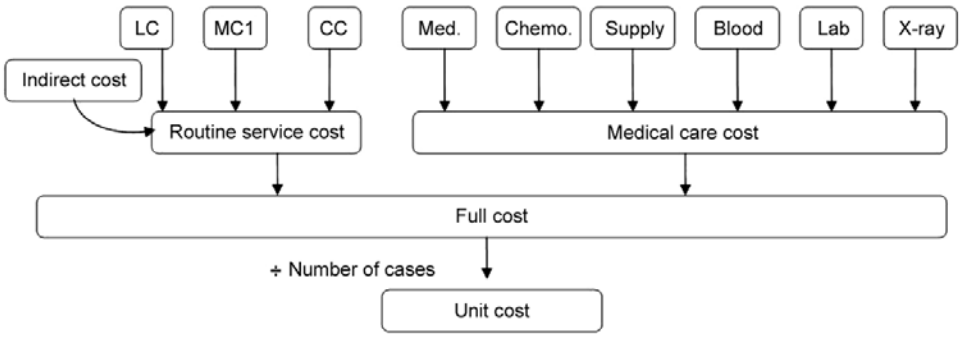

Fig. 1 All components of total costs of HSCT
LC = labor costs
MC1 = general material costs (except drugs and medical supplies)
CC = capital costs
Indirect cost = costs allocating from non-revenue producing cost centers and revenue producing cost centers
Med = drug costs (except chemotherapeutic drugs)
Chemo = chemotherapeutic drug costs
Supply = medical supply costs
Blood = blood and blood-component costs
Lab = laboratory test cost
X-ray = Radiological investigation and radiation costs

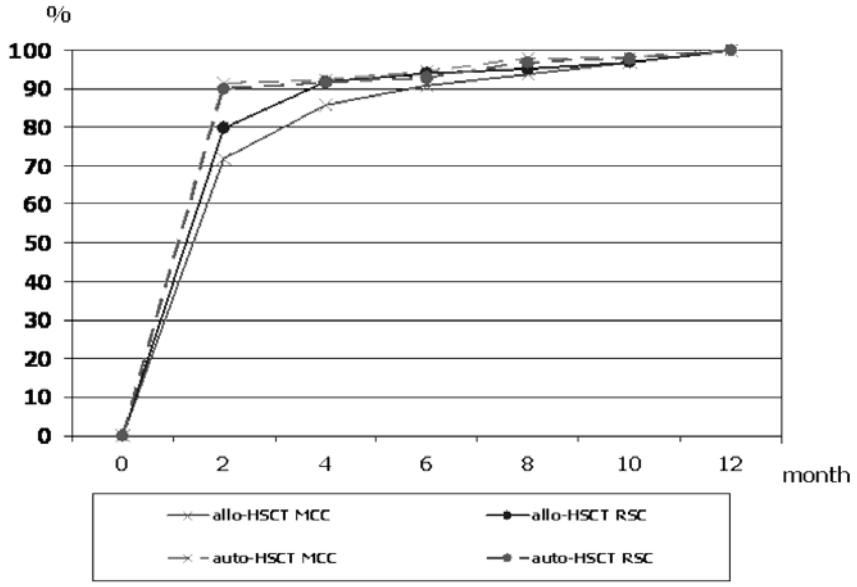

Fig. 2 Cumulative percentage of medical care cost and routine service cost of allo-HSCT and auto-HSCT

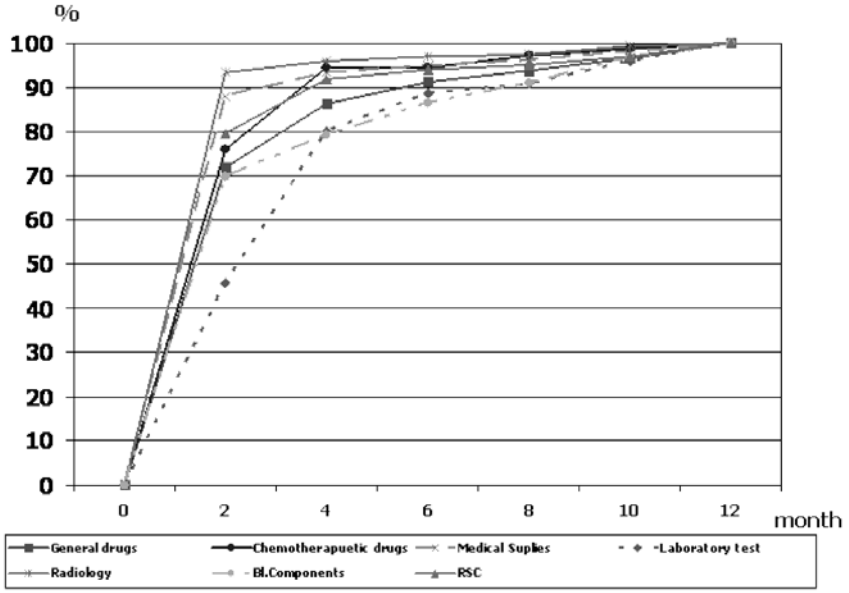

Fig. 3 Cumulative percentage of medical care cost of allo-HSCT

and 5th-6th month ($576 and $467 per case per 2 month, respectively). Furthermore, utilizing the agents to stimulate or elevate red blood cells, white blood cells or platelets, such as Recormon, Intron A, Eprex, intravenous infusion of immonoglobulin (IVIG), were the other reasons for the higher costs.

In-patient MCC for allo-HSCT for harvesting of marrow (1st-2nd month) in allo-HSCT was higher than auto-HSCT at the same time ($10,227 compared to $9,105 per case per 2 months). The reasons of this higher cost were administrating the conditioning regimen in order to eradicate the patient's disease and provide adequate

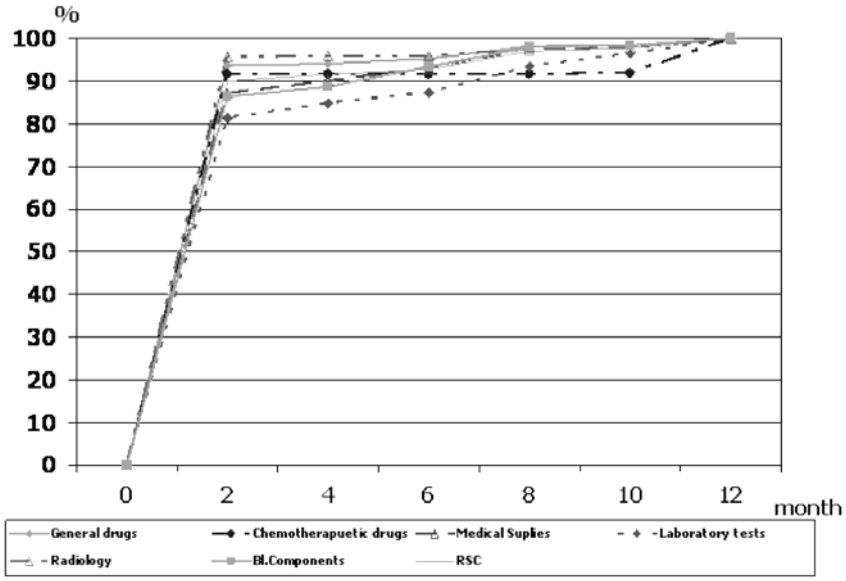

Fig. 4 Cumulative percentage of medical care cost of auto-HSCT

immunosuppression for preventing rejection of the graft[11] and analyzing drugs level of cyclosporin, until proper condition is obtained.

MCC of auto-HSCT is higher than allo-HSCT in the 5th-6th month because of febrile neutropenia, especially during relapse stage. Various treatments of febrile neutropenia, such as antibiotics, antifungal drugs (Ambisome), and human granulocyte colony-stimulating factor (G-CSF) for stimulating neutrophil, drove the drug costs higher.

Total MCCs of IP per case per year of auto-HSCT was slightly higher than allo-HSCT ($12,011.23 compared to $11,913.10 per case). Febrile neutropenia was the main cause of higher cost in auto-HSCT which required prolonged hospitalization.

Allo-HSCT is more expensive than auto-HSCT and this may be due to the higher MCC of allo-HSCT. Labor cost, a component of RSCs, is difficult to determine. Another reason for confusion is separated payment of insurance scheme. UC scheme has designed two channels, chemotherapeutic-agents costs, and other overall costs, of reimbursement. Chemotherapeutic-agents costs obviously appear on the billing documents. Conversely, the other overall costs are reported with the fixed rate of hospital costs per day where as not more than $2.64. The authors can, therefore, not clearly know the exact costs of RSCs.

The total costs of HSCT in the present study were much lower than in previous studies from the Western countries which were between $63,398 and $104,480[3, 12-14]. The major reasons for these differences were different components of costs which included professional fees and logistic costs. Most of the studies from other countries were longitudinal designs, such as five, seven or ten years of follow up and cost calculation. However, the issue that auto-HSCT was higher than allo-HSCT was similar to result from a previous study[1].

Although the numbers of subjects were small due to financial barriers, the present study revealed a high total cost of HSCT in the first year. The present study was not designed to assess effectiveness of transplantation procedures for different indications, although it is important to consider both economics and clinical results when determining health care policy. Several studies had found that allo-HSCT was cost-effective because it yielded a longer quality-adjusted survival despite the higher overall costs of HSCT[15,16]. Further research is necessary to investigate the cost-effectiveness or cost-utility of HSCT compared with chemotherapy which is a recent gold standard of UC scheme for AML in Thai patients. This evaluation of the economic burden in the treatment of AML patients should help to establish a support policy.

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Abbreviations

allo-HSCT:	allogeneic bone marrow transplantation	IP:	in-patient
AML:	acute myeloid leukemia	KCMH:	King Chulalongkorn Memorial Hospital
auto-HSCT:	autologous bone marrow transplantation	LOS:	length of stay
BMT:	bone marrow transplantation	MCC:	medical care cost
CR:	complete remission	OP:	out-patient
CSMBS:	civil servant medical benefit scheme	PBSCT:	peripheral blood stem cell transplantation
DMP:	disease management program	RSC:	routine services cost
DRG:	diagnosis-related group	SSS:	social security scheme
HLA:	human leukocyte antigen	UC:	universal coverage
HSCT:	hematopoietic stem cell transplantation		

การวิเคราะห์ต้นทุนการปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดในผู้ป่วยมะเร็งเม็ดเลือดขาวมัยอีลอยด์ชนิดเฉียบพลันผู้ใหญ่ ณ โรงพยาบาลจุฬาลงกรณ์

สุรีรัตน์ งามเกียรติไพศาล, จิรุตม์ ศรีรัตนบัลล์, ภิรมย์ กมลรัตนกุล, ธานินทร์ อินทรกำธรชัย, นภดล นพคุณ, พงษ์พิสุทธิ์ จงอุดมสุข

การศึกษานี้มีวัตถุประสงค์เพื่อวิเคราะห์ต้นทุนในปีแรกของการปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดในการรักษาผู้ป่วยมะเร็งเม็ดเลือดขาวมัยอีลอยด์ชนิดเฉียบพลัน ผู้ใหญ่ หรือ AML ณ โรงพยาบาลจุฬาลงกรณ์ รูปแบบการศึกษาเป็นการศึกษาย้อนหลัง ในผู้ป่วย AML จำนวน 67 ราย ที่ได้รับการปลูกถ่ายไขกระดูกที่โรงพยาบาลจุฬาลงกรณ์ ระหว่างปี พ.ศ. 2537-2548 การเก็บข้อมูลต้นทุนที่ใช้จริงได้จากการทบทวนเวชระเบียนผู้ป่วยเมื่อรวบรวมต้นทุนค่าบริการทางการแพทย์ ส่วนข้อมูลค่าบริการพื้นฐานนั้น ใช้ข้อมูลจากรายงานการวิเคราะห์ต้นทุนรายปีของโรงพยาบาลจุฬาลงกรณ์ มาปรับ โครงสร้างต้นทุนให้เหมาะสม ต้นทุนรวมนี้ได้รับการปรับให้เป็นค่าเงินของปี 2549 ด้วยดัชนีราคาผู้บริโภค จากการศึกษา พบว่าต้นทุนของการปลูกถ่ายเซลล์ต้นกำเนิดชนิดใช้เซลล์จากพี่น้องเท่ากับ $22,592.85 และของการปลูกถ่ายเซลล์ ต้นกำเนิดชนิดใช้เซลล์ตนเองเท่ากับ $24,171.25 ในปีแรก ส่วนการประเมินต้นทุนประสิทธิผลโดยการเปรียบเทียบกับ การรักษาด้วยเคมีบำบัดจำเป็นต้องมีการศึกษาต่อไป