Predictors of Outcome after Open Repair of Ruptured Abdominal Aortic Aneurysms

Hao-Jui Li, MD; Tsung-Chi Kao, MD; Dah-Wel Liu, MD; Sheng-Yueh Yu, MD; Po-Jen Ko, MD; Hung-Chang Hsieh, MD

Background: To determine predictors associated with early hospital death, 30-day mortality, and long-term survival after open surgical treatment of ruptured abdominal aortic aneurysms (RAAAs).

Methods: A retrospective chart review of 127 consecutive patients who received open surgical treatment of a RAAA at Chang Gung Memorial Hospital, Taiwan, from February 1994 to May 2007. Data recorded included patient characteristics, medical history, perioperative variables, and outcomes.

Results: There were 104 men and 23 women with a mean age of 70 ± 12 years in the analysis. Patients with RAAAs were classified into two groups; 100 (78.7%) patients were classified as group I (hemodynamically stable), and 27 (21.3%) patients were classified as group II (hemodynamically unstable at arrival). The 30-day mortality was 22% for group I and 74.1% for group II. Multivariate analysis identified age > 75 years old (odds ratio [OR], 0.083; 95% confidence interval [CI] 0.02-0.36), hemodynamically unstable state (OR, 0.081; 95% CI 0.016-0.4), blood transfusion > 5 L (OR, 0.14; 95% CI 0.038-0.54), intraperitoneal rupture (OR, 7.2; 95% CI 1.4-36), urine output < 0.5 mL/kg/min (OR, 22; 95% CI 4.6-110), and suprarenal cross-clamping (OR, 0.083; 95% CI 0.019-0.36) as incremental risk factors for 30-day mortality.

Conclusion: Significant predictors of mortality in patients with RAAAs include hemodynamically unstable state, age > 75 years old, intraperitoneal rupture, low intraoperative urine output, and suprarenal cross-clamping.

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Key words: ruptured abdominal aortic aneurysm (RAAA)

Abdominal aortic aneurysm (AAA) is a common disease in Western countries, occurring in 1 in 20 elderly men who have smoked at some time in their lives.[1] A recent population-based study indicated that the incidence of ruptured AAA (RAAA) increased from 5.6 per 100,000 person-years for time period from 1971 to 1986 to 10.6 per 100,000 person-years for 2000 to 2004 despite a 100% increase in elective repairs.[2] Rupture of an AAA has a mortality rate of 80% and causes 9000 deaths per year in the United States.[3,4] AAA, however, is unusual in Eastern countries, and in Taiwan only 575 patients

From the Division of Vascular Surgery, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Taoyuan, Taiwan.
Received: Jan. 21, 2010; Accepted: July 26, 2010
Correspondence to: Dr. Hao-Jui Li, Division of Vascular Surgery, Chang Gung Memorial Hospital at Linkou. 5, Fusing St., Gueishan Township, Taoyuan County 333, Taiwan (R.O.C.) Tel: 886-3-3281200 ext. 2148; Fax: 886-2-87126988;
E-mail: r2917@ms16.hinet.net

(2.6 per 100,000 person-years) died from an aortic aneurysm in 2006.[5] Mortality for conventional repair of a RAAA has remained largely unchanged over the past decade. A recent meta-analysis revealed a perioperative mortality of 48% in patients who underwent open repair.[6] Similarly, a United States study indicated a perioperative mortality rate of 52% for open repair.[7] There are, however, few studies reporting the mortality of open treatment of RAAA in Asian countries.[8-10]

In Western countries, endovascular aneurysm repair (EVAR) has been a promising procedure for the treatment of AAA. Although studies appear to indicate that EVAR of RAAA is safe and effective for selected patients, there seems to be little difference in the 30-day mortality compared with an open approach.[11,12] Because the costs of EVAR has previously not be covered by national health insurance in Taiwan.

The purpose of this study is to report our experience with conventional open repair of RAAA, analyze the perioperative risk factors associated with increased mortality, and compare the results with published studies of RAAAs managed with EVAR.

METHODS

In this retrospective chart review, we analyzed the records of 127 consecutive patients who received conventional open repair of a RAAA below the level of the renal arteries at our hospital from February 1994 to May 2007. Patients with acute or symptomatic but intact AAA identified on computed tomography (CT) were excluded.

Preoperative data recorded included gender, age, the presence of hypertension, heart disease, renal disease, diabetes mellitus, and chronic obstructive pulmonary disease (COPD), Charlson comorbidity index, hematocrit, blood pressure at admission to the emergency department (ED), serum creatinine level, and size of the aneurysm. Intraoperative data recorded included blood pressure at arrival in the operating room (OR), the level of aortic cross-clamping, graft used, blood volume transfused, total fluid transfused, blood loss, and urine output.

The diagnosis of RAAA was based on the detection of extraluminal hemorrhage in the retroperitoneum and/or intraperitoneal space by CT scan or ultrasound. All patients underwent RAAA repair through a transperitoneal approach with general anesthesia. An emergency operation was defined as surgery within 6 hours of the patient's arrival in the ED. An urgent operation was defined as surgery conducted more than 6 hours after, but within 24 hours of the patient's arrival in the ED. A regular operation was defined as surgery performed more than 24 hours after the patient arrived in the ED. Immediate mortality was defined as death occurring during surgery or within 24 hours after surgery.

Patients were divided into two groups for comparative analysis according to their hemodynamic status at presentation to the hospital ED.[11] Group I patients were hemodynamically stable which was defined as the patient being conscious and/or having a systolic blood pressure ≥ 80 mm Hg, with or without fluid resuscitation. Group II patients were hemodynamically unstable which was defined as unconscious and/or having a systolic blood pressure < 80 mm Hg after fluid resuscitation.

Statistical analysis

Continuous variables were presented as the mean ± standard deviation (SD). Univariate analysis was conducted with Student's *t*-test for comparison of continuous variables. The chi-square test was used for analysis of the prevalence of risk factors. Risk factors that were found to be significant were entered into multivariate analysis performed with binary logistic regression analysis for predicting perioperative mortality (within 30 days). Kaplan-Meier method estimates of the survival rate distribution were generated for all patients and for the two groups. Risk ratios and 95% confidence internals (CIs) were calculated to determine the risk at any point in time for the index group in comparison with the reference set. A value of $p < 0.05$ was considered to indicate statistical significance.

RESULTS

There were 127 patients, 104 men (81.9%) and 23 women (18.1%), ranging in age from 18 to 94 years (mean, 70.4 ± 12 years) included in the analysis. Patient characteristics, comorbidities, and operative data for the whole cohort and by subgroup are presented in Table 1. Patient symptoms on admission are presented in Table 2. The most common presenting symptom was abdominal pain in 89 patients

Table 1. Patient Characteristics, Comorbidities, and Operative Data

Variable	Group I (n = 100)	Group II (n = 27)	p value
Male	83 (83.0)	21 (77.8)	NS
Age (years)	69 ± 13	73 ± 8	NS
Mean aneurysm diameter (cm)	6.8 ± 1.8	6.8 ± 1.4	NS
Comorbidity index	1.5 ± 1.4	2.03 ± 1.4	NS
Hypertension	52 (52.0)	13 (48.1)	NS
Heart disease	11 (11.0)	6 (22.2)	NS
Diabetes mellitus	21 (21.0)	3 (11.1)	NS
COPD	11 (11.0)	2 (7.4)	NS
Hematocrit (%)	31 ± 8	29 ± 6	NS
Serum creatinine (mg/dL)	1.6 ± 0.7	1.8 ± 0.6	NS
BP in ER (mm Hg)	120 ± 28	67 ± 33	< 0.001*
BP in OR (mm Hg)	120 ± 33	93 ± 37	< 0.001*
Duration of surgery (min)	330 ± 140	300 ± 100	NS
Blood transfusion (units)	17 ± 15	27 ± 15	0.003*
Total fluid during surgery (mL)	3,900 ± 3,000	3,500 ± 2,000	NS
Intraperitoneal rupture	15 (15.0)	9 (33.3)	0.043*
Blood loss (mL)	5,000 ± 1,000	6,000 ± 1,200	NS
Suprarenal cross-clamping	23 (23.0)	11 (40.7)	NS

Continuous data are expressed as mean ± SD and tested with Student's t-test.

Categorical data are expressed as number (%) and tested with the chi-Square test.

Abbreviations: NS: not significant; COPD: chronic obstructive pulmonary disease; BP: blood pressure; ED: emergency department; OR: operating room; *: $p < 0.05$.

Table 2. Presenting Signs and Symptoms of Ruptured Abdominal Aortic Aneurysms (N = 127)

	No.	Percent
Abdominal pain	89	70.1
Shock	24	18.9
Back pain	16	12.6
Fever	14	11.0
Loss of consciousness	11	8.7
Flank pain	9	7.1
Abdominal mass	3	2.4
Chest pain	2	1.6
Epigastric pain	2	1.6
Constipation	2	1.6
Dyspnea	2	1.6
Vomiting	1	0.8
Bloody stool	1	0.8
Weakness	1	0.8
Cold sweats	1	0.8
Leg pain	1	0.8

(70%), followed by shock in 24 (18.9%), and back pain in 16 (12.6%). Emergency operations were performed in 76 patients (59.8%), urgent operations in 31 (24.4%), and regular operations in 20 (15.7%). There were 80 patients who presented with abdominal pain received emergenct or urgent surgery, whereas 20 patients (with or without abdominal pain) did not receive an emergenct or urgent operation. The mean diameter of the aneurysms was 6.8 ± 1.7 cm. The mean Charlson comorbidity index was 1.6 ± 1.4.[13] There were 65 patients (51.2%) with hypertension, 32 (25.2%) with renal diseases including 30 patients (23.6%) with renal insufficiency (serum creatinine > 2 mg/dL), 24 (18.9%) with diabetes mellitus, and 17 patients (13.4%) with a history of heart disease. Other comorbidities are summarized in Table 2.

In total, 93 (73.2%) patients had aortic cross-clamping at an infrarenal site. Seventeen patients (13.3%) required suprarenal cross clamping and 17 patients (13.3%) required transthoracic cross-clamping. Straight grafts were used in 61 (48.0%) patients, whereas aortobiiliac (n = 23), aortobifemoral (n = 13), aortoiliac/femoral bifurcation (n = 7), and extra-anatomic bypass grafts (n = 23) were used less frequently.

Seventeen patients died during or within 24 hours after surgery giving an immediate mortality rate of 13.3%. Forty-two deaths occurred from 24 hours to 30 days after surgery, leading to a total 30-day mortality rate of 33.1%. The total in-hospital mortality rate was 38.6%. Group II patients had significantly higher immediate, 30-day, and in-hospital mortality rates (33.3%, 74.1%, and 74.1%, respectively) than group I patients (8.0%, 22.0%, and 29.0%, respectively). The 95% CIs for the differences in mortality rates between the two groups were 10.8% to 39.8% for immediate mortality, 32% to 72% for 30-day mortality, and 24.4% to 68.5% for

in-hospital mortality. The postoperative re-intervention rate was 17.3%, with no significant difference between groups I and II (19% vs. 11.1%) (Table 3).

The total length of hospital stay was 35 ± 25 days (range, 8-149 days; median, 29 days) for the entire series. Forty-nine of the surviving patients (38.6%) had no complications. Major complications in survivors are presented in Table 3 and included respiratory failure in 5 patients (3.9%), multiple organ failure in 4 (3.1%), and upper gastroenteric bleeding in 4 (3.1%). Minor complications included three wound infections (2.4%), 2 wound dehiscences (1.6%), and one ventral hernia (0.8%) (Table 3).

The 30-day mortality rates of patients with various perioperative risk factors are presented in Table 4.

Table 3. Group Mortality and Morbidity Rates

Variable	Group I (n = 100)	Group II (n = 27)	p value
Immediate mortality (< 24 hours)	8 (8.0)	9 (33.3)	0.001*
30-day mortality	22 (22.0)	20 (74.1)	< 0.001*
In-hospital mortality	29 (29.0)	20 (74.1)	< 0.001*
Postoperative re-intervention	19 (19.0)	3 (11.1)	NS
Morbidities			
Wound problems	5	1	–
Respiratory failure	4	1	–
Multi-organ failure	4		–
Graft thrombosis	4		–
Gastrointestinal bleeding	3	1	–
Acute renal failure	3		–
Internal bleeding	1	1	–
Cerebrovascular accident	2		–
Acute myocardial infarct	1		–
Colon perforation	1		–
Ureter injury	1		–
Pleural effusion	1		–
Sepsis	1		–
Neutropenia	1		–
Jaundice	1		–

Data are expressed as numbers (%) and tested with the chi-Square test. The 95% confidence intervals for differences in the mortality rates between the two groups are 10.8% to 39.8% for immediate mortality, 32% to 72% for 30-day mortality, and 24.4% to 68.5% for in-hospital mortality; *: $p < 0.05$.

Results of multivariable analysis of the 30-day mortality are presented in Table 5. All variables were initially included in the multivariate analysis. Variables that were not significant in the univariate analysis remained not significant in the logistic regression analysis.

Table 4. Analysis of Perioperative Factors and 30-day Mortality

Risk factor	Odds ratio	95% CI	p value
Female gender	0.4	0.15-1.2	NS
Age > 75 years	2.0	1.3-3.1	0.002*
Hypertension	0.78	0.52-1.1	NS
Heart disease	0.84	0.32-2.2	NS
COPD	1.3	0.44-3.6	NS
Diabetes mellitus	0.41	0.15-1.1	NS
Hematocrit < 27%	1.6	0.97-2.6	NS
Serum creatinine > 2 mg/dL	2.1	1.2-3.7	0.007*
Aneurysm size > 8 cm	2.0	0.91-4.5	NS
Unstable state	5.9	2.7-12	< 0.001*
Comorbidity index > 2	2.1	1.3-3.7	0.007*
Blood loss > 5,000 mL	2.8	1.7-4.5	< 0.001*
Blood transfusion > 20 units	3.4	2.1-5.6	< 0.001*
Intraperitoneal rupture	4.0	1.9-8.7	< 0.001*
Suprarenal cross-clamping	2.9	1.6-5.1	< 0.001*
Straight graft	1.8	1.3-2.6	0.001*
Urine output < 0.5 mL/kg/min	7.4	3.3-17	< 0.001*

Abbreviations: NS: not significant; COPD: chronic obstructive pulmonary disease; *: $p < 0.05$.

Table 5. Multivariable Analysis of 30-day Mortality

Risk factor	Odds ratio	95% CI	p value
Age > 75 years	0.08	0.02-0.36	0.001*
Unstable state	0.08	0.02-0.40	0.002*
Blood transfusion > 20 units	0.14	0.04-0.54	0.004*
Intraperitoneal rupture	7.2	1.4-36	0.018*
Urine output < 0.5 mL/kg/min	22	4.6-110	< 0.001*
Suprarenal cross-clamping	0.08	0.02-0.36	0.001*

*: $p < 0.05$.

The mean patient follow-up was 37 ± 40 months (range, 2-160 months; median, 18 months). The 12-month cumulative survival of the entire group was 80 ± 4.5% (Kaplan-Meier) (Fig. 1). The 12-month Kaplan-Meier cumulative survival difference between groups I (80 ± 4.7%) and II (83 ± 15%) was not significantly different (Fig. 1).

DISCUSSION

Despite advances in surgical technique, RAAA continues to carry a high mortality. The incidence of RAAA is relatively rare in Asian countries compared with that in Western countries. The classic presentation of a RAAA is acute onset of pain in the abdomen, back, or both, followed by shock and the presence of a pulsatile abdominal mass; however, this typical presentation occurs in only 50% of patients.[14]

In this study, although abdominal pain was a presenting symptom in 70% of patients with RAAAs, only 18% presented with shock and 2% with an abdominal mass. Interestingly, there was no significant difference in 30-day mortality between the group that had abdominal pain and received an emergenct or urgent operation and the group that had neither abdominal pain nor an emergenct operation (21% vs. 13%). RAAA patients who presented with abdominal pain and received an emergency operation may have been in critical condition, partly explaining their higher mortality rate. Alternately, patients with an atypical presentation may have been misdiagnosed, thus delaying surgery and leading to a higher mortality rate.

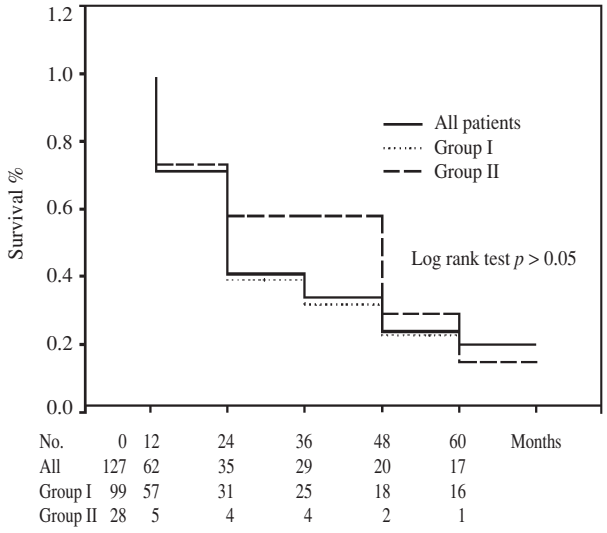

Fig. 1 Kaplan-Meier survival analysis comparing the cumulative survival rates between groups after open repair of a ruptured abdominal aortic aneurysm (log rank test, $p > 0.05$).

The overall 30-day mortality in this study was 33.1%, with an in-hospital mortality of 38.6%. These results are similar to findings in the recent meta-analysis of Hoornweg et al. who reported a 49% postoperative mortality.[15] They concluded that there has been no significant change in the mortality of RAAA over the last 15 years despite advances in diagnosis and treatment and that aging population may cause the result. This finding is comparable to the results of this study in which the age > 75 years was a risk factor for increased mortality.

In our study, the probability of a patient undergoing surgery for a RAAA was significantly lower for women than men (18% vs. 82%). The reason for this difference is unknown. A study by Dueck et al. indicated that men were more likely to undergo repair of a RAAA than women,[16] although the reasons for this were uncertain. Additionally, Dueck et al also found no difference in 30-day mortality based on gender. Despite the well-known fact that women have smaller diameter aortas than men,[17] similar aortic diameters are used to define thresholds for diagnosis and indications for surgery for AAA. However, our data showed that there was no difference in the size of RAAAs between men and women (6.7 ± 1.7 cm vs. 7.2 ± 1.5 cm). This result is contrary to the findings of the UK Small Aneurysm Trial published by Greenhalgh et al.,[18] in which the researchers found that the rate of rupture in women was 3 times the rate of rupture in men, and the mean diameter of the rupture was 5 cm in women and 6 cm in men. The problem of defining AAA based on diameter alone for women remains unresolved, and the concept of lowering the threshold size of the AAA for elective repair in women to prevent rupture is controversial.

We investigated the characteristics of stable and unstable patients to determine the reasons why the immediate, 30-day, and in-hospital mortality in unstable RAAA patients was more than 3 times higher than in stable patients. Of the characteristics examined, BP in the ED, BP in the OR, the amount of blood transfused, and the presence of intraperi-

toneal hemorrhage differed significantly between the two groups (Table 2). Rupture of an AAA most commonly involves the posterolateral aorta with hemorrhage into retroperitoneum. Intraperitoneal rupture may also occur, originating from the anterior or anterolateral aspect of the aneurysm. Retroperitoneal hemorrhage may be contained in the retroperitoneal space and a tamponade effect may help to slow blood loss. The patient may appear hemodynamically stable, leading to a false sense of security.

Intraperitoneal ruptures were specifically described in the surgical records, and were more common in group II than group I (33.3% vs. 15.0%, $p < 0.05$). We also found higher intraoperative blood loss in patients with intraperitoneal rupture and a larger volume of blood transfused in group II. These results suggest that intraperitoneal rupture is a major predictor of 30-day mortality in unstable patients.

The present study confirms age > 75 years, unstable state, blood transfusion > 20 units, intraperitoneal rupture, urine output < 0.5 mL/kg/min during surgery, and suprarenal cross-clamping are significant risk factors for 30-day mortality in patients with RAAA. Similar associations were identified by Turton et al., who weighted processing elements from the data of 102 consecutive patients with a RAAA to determine perioperative variables associated with poor outcome.[19] Their computerized neural network identified preoperative hypotension, intraperitoneal rupture, preoperative coagulopathy, and cardiac arrest as the 4 most significant risk factors for operative mortality.

Proximal aortic cross-clamping has been extensively used in the treatment of RAAAs because control of bleeding is the most important step in surgical management. The approach to early aortic cross-clamping varies and depends on several factors such as hemodynamic status (stable vs. unstable), the extent of hematoma, intraperitoneal rupture, and difficulty in controlling the aneurysm neck because of arteriosclerosis or adhesions. The majority of patients in our study underwent infrarenal cross-clamping, and we found that this was associated with significantly lower 30-day mortality than cross-clamping at other aortic sites ($p < 0.001$). The reason for this is unclear, especially given that there was no significant difference in blood loss or amount of blood transfused between patients who received and who did not receive infrarenal aortic cross-clamping.

We found that the long term survival did not differ between group II patients who survived beyond 30 days and group I patients (Fig. 1). These data were different from a previous report that indicated unstable patients had poorer long-term survival than stable patients.[11]

The adoption of EVAR in the treatment of RAAAs has been rapid because of its lower short-term mortality and morbidity rates and shorter length of hospital stay and recovery than with open repair. There is concern, however, that the long-term outcomes of emergenct EVAR for RAAAs may not be as good as those of open repair. Recently, Mastracci et al. reported a meta-analysis of EVAR for RAAA and found the in-hospital mortality for patients who underwent EVAR varied from 0% to 45% and pooled mortality was 21% (95% CI 13-29),[20] although the heterogeneity was high (90.2%). Study specific selection criteria indicated 47% of patients with RAAA were eligible for EVAR and the authors concluded that although mortality was lower than that in reports of unselected patients undergoing open repair, further investigation is needed to determine if the difference is attributable to patient selection or to the EVAR approach.

Coppi et al. found that the 30-day mortality of unstable and stable patients undergoing emergenct EVAR of RAAA was 53% and 11%, respectively.[11] In our study, the 30-day mortality of open treatment of a RAAA for unstable and stable patients was 74.1% and 22.0%, respectively. Compared to the results of Coppi et al., it appears there is no significant difference in open or EVAR treatment of RAAA. We believe that further evidence is required to consider EVAR as the first-choice treatment of RAAA and a randomized trial is needed to test the hypothesis that the patient's condition at presentation is the determining factor for survival, rather than the type of intervention chosen.

Conclusions

Mortality for patients with RAAA remains high despite advances in diagnosis and surgical techniques. Significant predictors of mortality include a hemodynamically unstable state, age > 75 years, intraperitoneal rupture, low intraoperative urine output, and suprarenal cross-clamping. Further randomized controlled study is needed to confirm the risk factors in the open treatment of RAAA.

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腹腔主動脈瘤破裂之開腹手術處理後之相關危險因子

李浩睿 高宗祺 劉大偉 游勝越 柯博仁 謝宏昌

背 景： 針對腹腔主動脈瘤破裂的病例，試圖找出可用於預估其死亡率的相關危險因子。

方 法： 1994 至 2007 年在長庚醫院共有 127 名腹腔主動脈瘤破裂的病例，以病歷回溯分析找出可能相關因子。病人之人口學資料，病史，手術期間以及預後的狀況均記錄並加以分析。

結 果： 127 位病人中共 104 位男性及 23 位女性，平均年齡爲 70 ± 12 歲。27 位 (21.3%) 到院時診斷爲不穩定型，另 100 位 (78.7%) 則爲穩定型。在不穩定型的病人中，其 30 天內死亡率爲 74.1%，而在穩定型的病人中之 30 天內死亡率則爲 22.0%。針對 30 天內死亡率的多變項分析的結果顯示，(1) 大於 75 歲，(2) 不穩定型，(3) 需要輸血量大於 5L，(4) 腹腔內破裂，(5) 排尿量 < 0.5 mL/kg/min 以及 (6) 腎下主動脈阻斷皆爲高死亡率危險因子。

結 論： 處理腹腔主動脈瘤破裂時，本研究發現的高死亡率危險因子可協助臨床醫師提高警覺，減少傷害程度並獲致良好預後。

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關鍵詞：破裂腹主動脈瘤

長庚醫療財團法人林口長庚紀念醫院 血管外科；長庚大學 醫學院
受文日期：民國99年1月21日；接受刊載：民國99年7月26日
通訊作者：李浩睿醫師，長庚醫療財團法人林口長庚紀念醫院 血管外科。桃園縣333龜山鄉復興街5號。
Tel: (03)3281200轉2148; Fax: (02)87126988; E-mail: r2917@ms16.hinet.net