PLATELET TRANSFUSION IN TRAUMA RESUSCITATION: EARLY HIGH RATIOS IMPROVE SURVIVAL IN QATAR

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Background

- Trauma remains a leading cause of death worldwide
- Most deaths occur early after admission and are caused by early exsanguinating hemorrhage
- 'Coagulopathy of trauma' sets in early
- Aggressive blood component therapy, in the form of MTP's, has replaced the crystalloid dependent fluid resuscitation

How Much ??? How early ???

- Controversy –

  - optimal ratio of platelets to PRBC in trauma patients requiring massive transfusion

  - the time at which the best ratio is achieved.

Aim

- To describe the effect of attaining a high Platelet: PRBC ratio ≥ 1: 1.5, within ***four hours***, on a trauma population receiving MT.

Study Design

- Retrospective chart review from 2010-12
- Hamad Trauma Center, the national Level I trauma referral center in Qatar.
- Inclusion: all adult patients [≥ 18 years] with traumatic injury who received massive blood transfusion ≥10 units of PRBC over initial 24 hours
- Platelet: PRBC ratio of

  > 1:1.5 at four hours post-injury - high ratio group

  ≤ 1: 1.5 at four hours post-injury - low ratio group

- The ratios were then calculated based on the blood products given from 4 to 24 hours post injury.
- Patients were followed up to 30 days, hospital discharge or death; whichever occurred earlier.
- Outcomes measured included overall mortality, multi-organ failure [MOF] and infectious complications.

- Data was analyzed using Chi-square and Student's T-test.
- All data were summarized as mean _ SD, median (interquartile range), or percentage (%).
- A two-sided p-value of >0.05 was considered to be statistically significant.

Results

- 4864 trauma admissions
- 100 [2.06%] patients met inclusion criteria
- Platelet: PRBC ratios attainable in 58 patients
- Median age - 32.3 years
- Median ISS of 31.9
- RTS of 5.1
- Blunt trauma accounted for most cases (84.5%).
- The overall mortality for the group was 69%

Age (years)	32.3±10.7
Gender	52 (91.2%)
Blunt trauma	49 (84.5%)
Mechanism of injury	
Traffic Pedestrian	13 (22.45)
Traffic Driver	16 (27.6%)
Traffic Passenger	9 (15.5%)
Fall From Height	9 (15.5%)
fall of heavy object	4 (6.9%)
Gunshot	2 (3.4%)
Stab	4 (6.9%)
SBP (mmHg)	81.1±31.8
HR (b/min)	123.6±25.9
Temperature in ED (°C)	36.12±0.69
FAST (+ve)	34 (58.6%)
Hb initial (g/dL)	10±2.7
Platelets initial ($\times 10^9$/L)	182±67.4
INR (initial)	1.7±1.4
APTT (initial) (s)	38.9 (23-911)
Fibrinogen initial (g/L)	0.75±0.6
pH	7.1±0.2
HCO3 initial (mmol/L)	14.5±4.6
ISS	31.9±11.5
RTS	5.1±2.2
GCS	4.2±3.5
ICU LOS	2.5 (1-44)
Hospital LOS	(1-255)
Mortality	40 (69%)

Table 2: Baseline comparison of clinical characteristics by group			
	Plt : PRBC ≥1:1.5 n=19	*Plt : PRBC <1:1.5 n=39*	*p value*
Age (mean±SD)	32.7±10.2	31.9±11.3	0.822
Blunt injury (%)	89.5	82.1	0.377
Penetrating injury (%)	10.5	17.9	
Initial Hemoglobin (mean±SD)	10.5±2.4	9.8±2.8	0.373
Initial INR (mean±SD)	1.4±0.4	1.9±1.7	0.351
Initial pH (mean±SD)	7.2±0.1	7.1±0.2	**0.007**
ISS (mean±SD)	29.3±11.6	33.1±11.3	0.254
RTS (mean±SD)	5.1±2.4	5.1±2.1	0.932

Table 3: A comparison of select laboratory and clinical outcomes, by group			
	Plt : PRBC ≥1:1.5 n=19	*Plt : PRBC <1:1.5 n=39*	*p value*
Hyperkalemia (%)	11.1	33.3	0.077
Hypomagnesemia (%)	68.8	61.5	0.493
Hypocalcemia (%)	77.8	84.4	0.413
ACS (IAP) (%)	5.3	5.1	0.704
Multi Organ Failure (%)	42.1	87.2	0.001
VAP (%)	38.9	10.8	0.021
Wound infection (%)	50	10.8	0.002
BSI (%)	11.1	10.8	0.649
CLI (%)	5.6	5.4	0.704
UTI (%)	0	5.4	0.448
Overall Mortality (%)	36.8	84.6	0.001

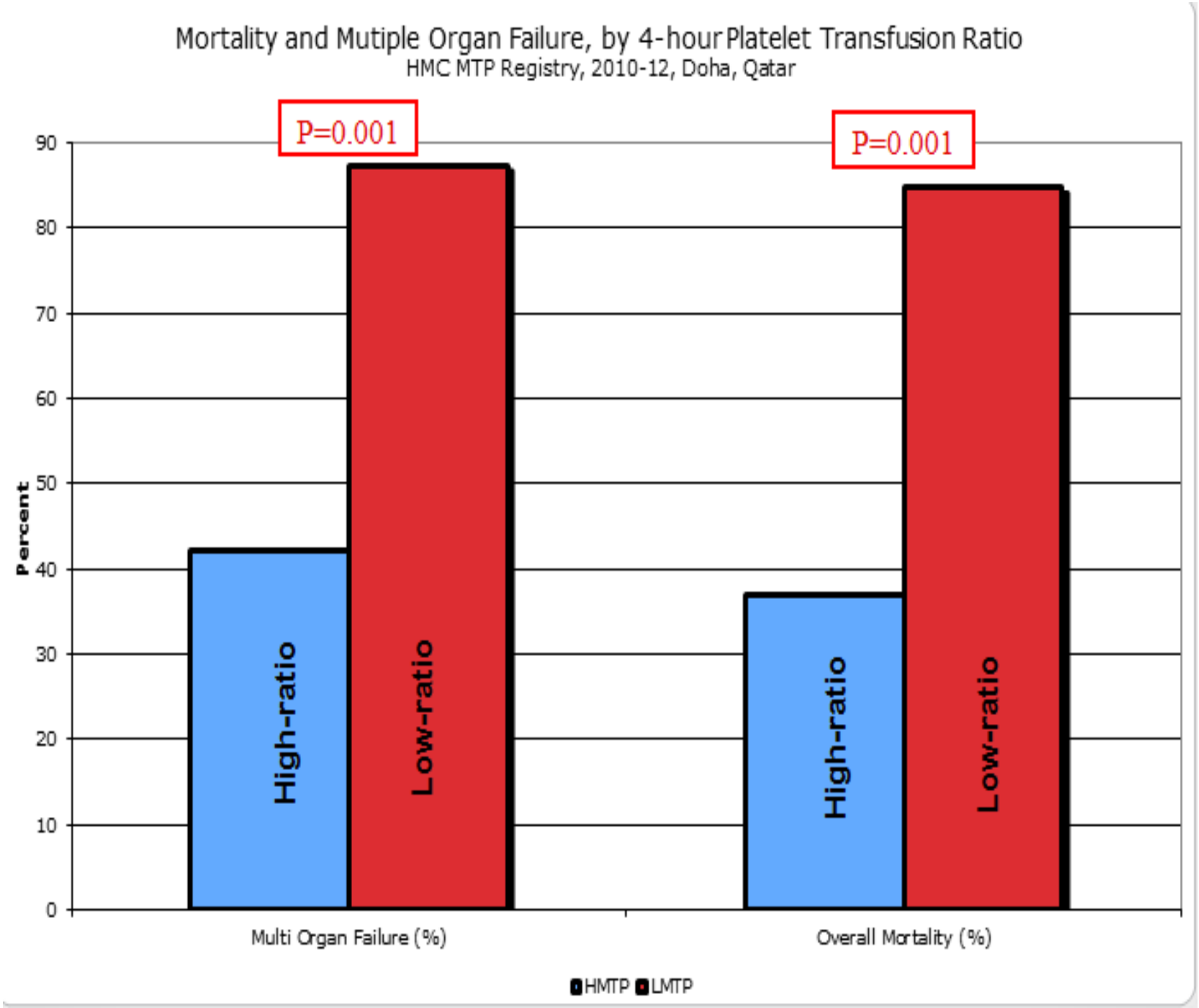
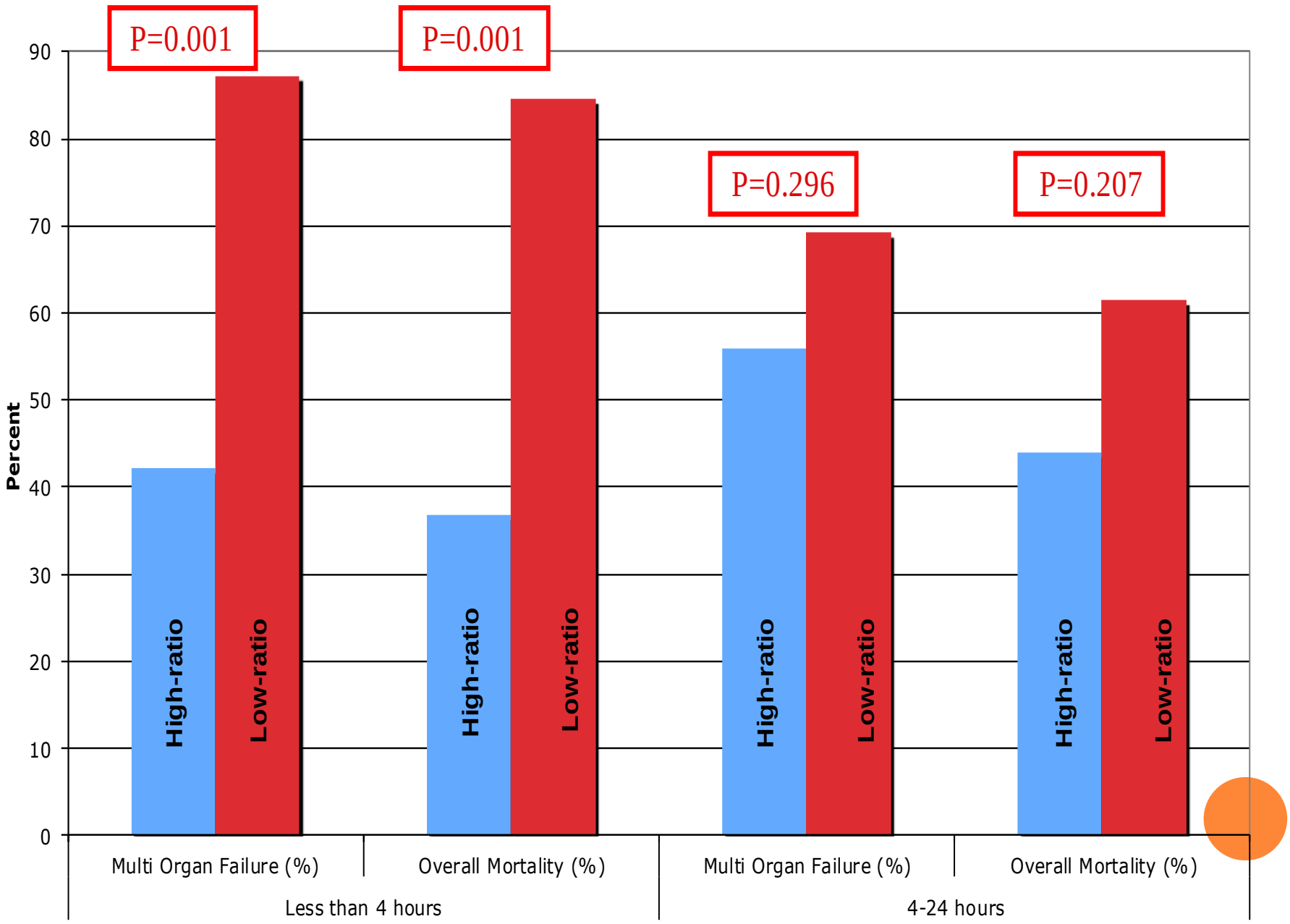
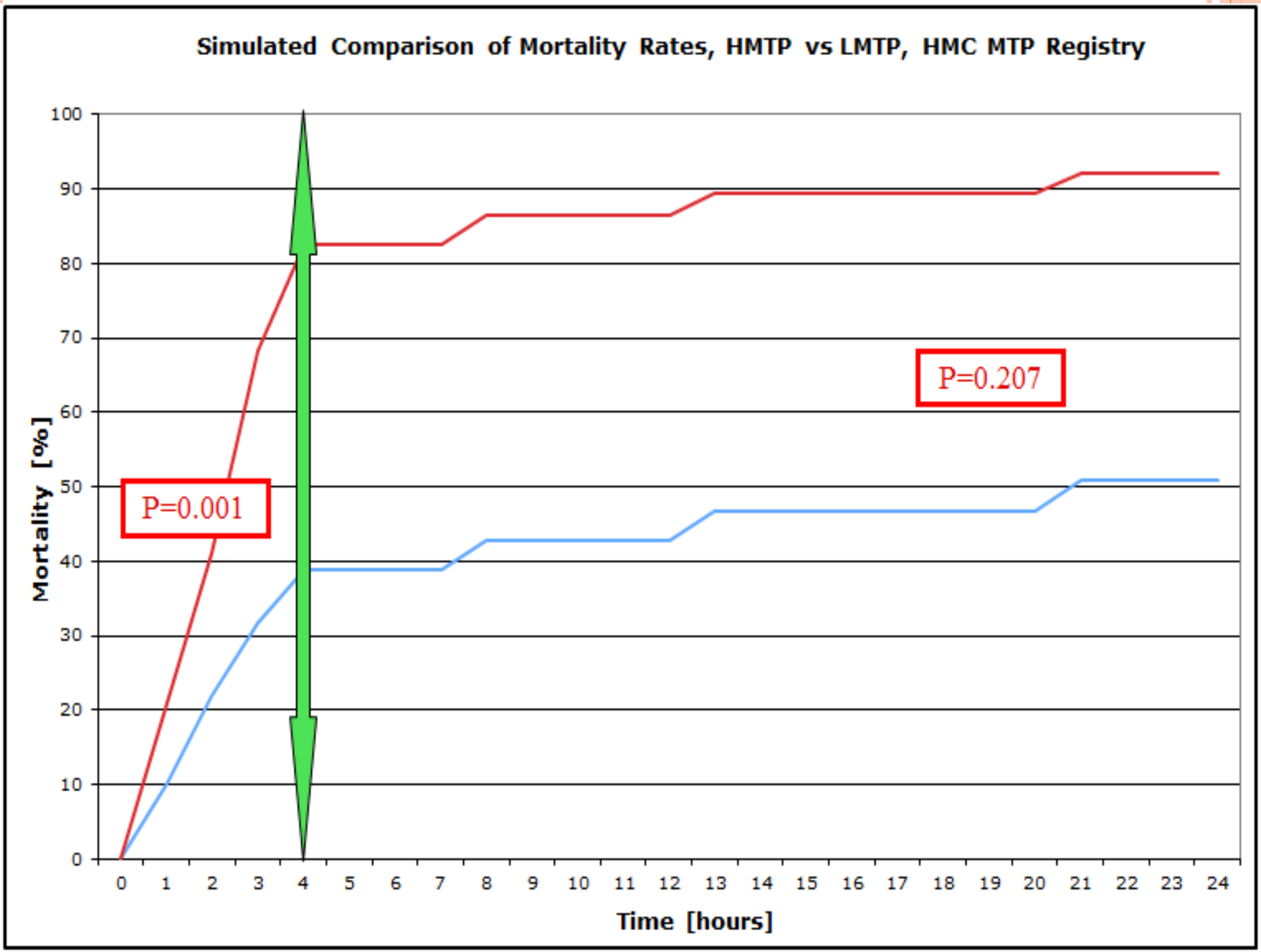

Mortality and Mutiple Organ Failure, by 4-hour Platelet Transfusion Ratio
HMC MTP Registry, 2010-12, Doha, Qatar
P=0.001
P=0.001
90
80
70
60
50
40
30
20
10
0
Percent
High-ratio
Low-ratio
High-ratio
Low-ratio
Multi Organ Failure (%)
Overall Mortality (%)
HMTP
LMTP

Table 4 : Comparative studies						
Reference	No	Mechanism	Massive transfusion	Time ratio calculated	Platelet : PRBC	Results
Holcomb et al, 2008	466	35% penetrating	≥ 9 U RBC in 1st 24 hr	24 hr	low ratio < 1 : 2 high ratio ≥ 1 : 2	Improved 30-day survival in high ratio
Gunter et al. 2008	259	55% penetrating	≥10 U RBC in 1st 24 hr	24 hr	low ratio < 1 : 1.5 high ratio ≥ 1 : 1.5	reduction in 30-day mortality in the high ratio group
Dente et al 2009	73	60% blunt	≥10 U RBC in 1st 24 hr	24 hr	High (1:1–2:1) Med (2:1–3:1) Low (>3:1)	higher ratios were associated with improved survival at 24 hours.
Inaba et al, 2010	657	55% penetrating	≥10 U RBC in 1st 24 hr	12, 24 hr	Low (<1:3), Med (≥1:3 & <1:2), High (≥1:2 & <1:1), Highest (≥1:1).	higher ratios were associated with improved survival at 24 hours.
Holcomb et al, 2011	643	66% blunt	≥10 U RBC in 1st 24 hr	6, 24 hr	Low > 1:20 Mid 1:2 High 1:1	High ratio was associated with improved early and late survival
Brown et al, 2012	604	100% blunt	≥10 U RBC in 1st 24 hr	6, 12, 24 hr	low ratio < 1 : 1.5 high ratio ≥ 1 : 1.5	higher ratios were associated with improved survival at 24 hours.


Mortality and Multiple Organ Failure Rates, by time and MTP ratio
HMC MTP Registry, 2010-12, Doha, Qatar
P=0.001
P=0.001
P=0.296
P=0.207
Percent
90
80
70
60
50
40
30
20
10
0
High-ratio
Low-ratio
Multi Organ Failure (%)
Overall Mortality (%)
Less than 4 hours
4-24 hours


Simulated Comparison of Mortality Rates, HMTP vs LMTP, HMC MTP Registry
Mortality [%]
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time [hours]
P=0.001
P=0.207

Platelet Plateau Phenomenon

- We believe that the survival benefit of attaining a high Platelet: PRBC ratio at 24 hours is heavily influenced by the attainment of such at 4 hours.

- Therefore in this study population, the impact of an MTP was in the attainment of a 'platelet plateau', consisting of the early administration of the platelets at an optimum ratio [≥1:1.5] within 4 hours from injury.

Inference

- The aggressive attainment of high Platelet: PRBC ratios as early as 4 hours post injury can substantially improve coagulopathy, and reduce mortality and multi-organ failure rates in severely injured patients.

- The high ratio group patients were associated with a higher wound infection and pneumonia rates. These are probably attributable to the severity of the underlying injury to compound the potential for a contributory immunodeficiency from this type of resuscitative practice.

Conclusion

- Survival advantage for trauma patients is realized EARLY.

- The attainment of this ‘platelet plateau’ should be the focus of subsequent clinical research.

Merci Beaucoup....

Definitions

- The diagnosis of multiple-organ failure (MOF) required a maximum Marshall Multiple Organ Dysfunction score > 5
- Diagnosis of ventilator-associated pneumonia [VAP] was based on the US National Nosocomial Infection Surveillance guidelines
- Diagnosis of catheter-related blood stream infections required positive peripheral cultures with the identical organism obtained from either a positive semi-quantitative culture (≥15 CFU/segment), or positive quantitative culture (≥103 CFU/segment) from a catheter segment specimen.
- Urinary tract infections required ≥105 organisms/ml of urine.

Table 2: Analysis for the 4-24 hours			
	Plt : PRBC ≥1:1.5 n=50	***Plt : PRBC <1:1.5 n=13***	***p value***
Age (mean±SD)	36±15.3	30.1±8	0.118
Blunt injury (%)	96	77	0.055
Penetrating injury (%)	4	23	
ISS (mean±SD)	27.4±9.7	27.7±7.2	0.921
RTS (mean±SD)	5.7±1.9	4.4±2.2	0.082
Hyperkalemia (%)	12.2	23	0.279
Hypomagnesemia (%)	54.8	66.7	0.393
Hypocalcemia (%)	87.8	92.3	0.544
ACS (IAP) (%)	4	0	0.627
Acute Renal Failure (%)	10	7.7	0.639
Multi Organ Failure (%)	56	69.2	0.296
VAP (%)	36.7	38.5	0.576
Wound infection (%)	42.9	30.8	0.323
BSI (%)	16.3	7.7	0.390
CLI (%)	8.2	15.4	0.369
UTI (%)	8.2	7.7	0.720
Crude Mortality (%)	44	61.5	0.207
Initial Hemoglobin (mean±SD)	10.7±2.5	8.5±3	0.007
Initial base deficit (mean±SD)	-8.8±4.8	-15.9±4.8	0.001
Initial lactate (mean±SD)	5.8±4.2	10.3±5.9	0.021
Initial INR (mean±SD)	1.2 (1-3)	1.8 (1-10)	0.009
Initial pH (mean±SD)	7.21±0.1	7.1±0.2	0.024

Descriptive analysis of patients who needs Massive blood transfusion (MTP) (n=100)			
Males	90.8	**Spleen**	
Age	34±13.6	Grade 1	9
Nationality		Grade 2	2
Arab- (Non Qatari)	16.5	Grade 3	5
Non-Arabs	69.6	Grade 4	3
Qatari	13.9	Grade 5	6
Blunt injury	89	**Liver**	
Mechanism of injury		Grade 1	13
Stab	5	Grade 2	4
Traffic Pedestrian	25	Grade 3	4
Traffic Driver	28	Grade 4	6
Traffic Passenger	17	Grade 5	3
Gunshot	3	Aortic	5
Fall From Height	11	**IVC**	5
fall of heavy object	9	Major Vascular injury other than Aorta/IVC	24
crush injury	1	Cardiac	4
No protective measures	95	Pericardial	2
Place of injury		Bowel	19
Road	72	Mesentery	24
Home	9	Stomach	5
Work	18	Pancreatic	11
EMS		Bladder	7
Intubation	34.3	Kidney	8
CPR	5.1	Operative procedure	
Needle Thoracostomy	5.1	Exploratory Laparotomy	62
Splinting	28.6	Thoracotomy	21
Trauma Room		Chest tube	9
Intubation	48	Craniotomy	2
Unilateral Chest Tube	25	ORIF	4
Bilateral Chest Tube	17	External Fixation	8
FAST	50	Repair of major vessels/ nerves	22
Thoracotomy	2	Mangled extremity amputation	5
CPR	10	**Intra operative status**	
Angioembolization Timing		Stable + Procedure completion	18
<4 hrs	9	Stable + Damage control	37
4-24 hrs	5	Unstable + Procedure completion	1
Angioembolization Outcome		Unstable + Damage Control	27
Unsuccessful	3	**Intra operative mortality**	16
Successful	11	**Hyperkalemia**	21.7
Associated Injuries		**Hypomagnesemia**	60.9
Head	46	**Hypocalcemia**	87.9
Lung Contusion	63	**Hypothermia**	1
Hemothorax	37	**Acidosis**	99

Hepatitis C infection	**1.2**	**Platelet**	**10.3±6.5**
MRSA	5	FFP/PRBC ratio	1.01±0.7
VAP	24.7	Platelet/PRBC ratio	1.17±0.9
Wound infection	28.9	Cryoppt	10.7±4.7
BSI	9.3	Calcium Gluconate/Chloride mg	2101±1434
CLI	7.2	Sodium Bicarbonate	174.5±149.4
UTI	5.2	Fibrinogen	3140±1619
Mortality	58	Factor 7	6367±2478
Time of mortality		Adrenaline	6.6±5.2
< 6 hrs	28	Nor Adrenaline	7 (2-12)
6-12 hrs	11	Atropine	3.1±1.9
12-24 hrs	5	Ephidrine	16.5±10.8
24-48 hrs	4	Desmopressin	3.5±0.7s
48hrs-7days	8	**Initial**	
7-30 days	1	Hemoglobin	10.5±2.6
30-60 days	2	HCT	32±7.9
Time to TR (min)	68±38	WBC	17.5±7
Lowest GCS EMS	9±5.2	Platelet	199.3±78.6
Lowest SBP EMS	89.3±31.7	INR	1.5±1.1
Normal Saline EMS (ml)	1215±813	PT	16.1±12.9
Lowest GCS TR in 1st Hour	5.1±4.5	APTT	33.5 (22-911)
Lowest SBP TR in 1st Hour	70.7±26.2	Fibrinogen	0.8±0.4
Initial SBP in TR	87.2±33.4	pH	7.15±0.2
Initial HR in TR	118.4±26.7	PO2	189±126
ABC index	2.3±0.8	PCO2	45.5±15.9
Blood products/Crystalloids at 1st 4 hrs		BE	-11.7±6.4
Saline	3604±1503	HCO3	15.9±5.2
Ringer Lactate	1294±899	Corrected Ca	2±0.3
PRBC	9.6±5.3	Ionised Ca	1±0.2
FFP	6.5±3.8	Sodium	141±4.6
Platelet	6.2±3.4	Potassium	3.8±0.8
FFP/PRBC ratio	0.62±0.3	Creatinine	108.6±33.5
Platelet/PRBC ratio	0.56±0.25	Amylase	48.6±42.8
Cryoppt	8.7±3	Lipase	52 (20-506)
Calcium Gluconate/Chloride mg	2045±1477	Troponin T	22.9±50.3
Sodium Bicarbonate	126.3±89.8	Myoglobin	2438±1906
Fibrinogen	2750±1164	Bilirubin	7.4±5.4
Factor 7	4.5±1.8	ALT	59 (12-1471)
Adrenaline	6.2±3.9	AST	55 (27-518)
Nor Adrenaline	-	ALP	38.9±18.5
Atropine	2.4±1.3	Lactate	7.5±5.2
Ephidrine	27.5±23.7	Mg	0.7±0.1
Blood products/Crystalloids at 4-24 hrs		**First MTP**	
Saline	2478±1387	Hemoglobin	9.5±2.9

Platelet	**86.7±40.6**	**Myoglobin**	**2974±2833**
INR	1.4 (1-12)	Bilirubin	27.5±22.6
PT	14 (3-120)	ALT	46(14-1299)
APTT	61.6±43	AST	95(13-939)
Fibrinogen	1.1±0.6	ALP	45.7±18.2
pH	7.1±0.2	Lactate	6±5
PO2	192.7±153.6	Mg	0.7±0.2
PCO2	48±16.5	**Third MTP**	
BE	-10.7±6.3	Hemoglobin	8.8±2.4
HCO3	16.3±4.2	HCT	25±6.2
Corrected Ca	2±0.2	WBC	6±3.2
Ionised Ca	0.9±0.2	Platelet	82.4±32.7
Sodium	142.8±12.4	INR	1.1(1-10)
Potassium	4.5±0.9	PT	12(9-120)
Creatinine	98.2±31.4	APTT	51±33.3
Amylase	33±24.6	Fibrinogen	1.9±0.9
Lipase	44 (17-650)	pH	7.2±0.2
Troponin T	110 (1-634)	PO2	139±113
Myoglobin	3514±3417	PCO2	52.3±22.5
Bilirubin	14.6±11.7	BE	-8.3±6.6
ALT	36 (12-579)	HCO3	19.4±4.7
AST	65 (20-544)	Corrected Ca	1.9±0.4
ALP	45.6±20.9	Ionised Ca	1±0.4
Lactate	7.8±5	Sodium	151±8
Mg	0.7±0.1	Potassium	4.1±0.9
Second MTP		BUN	5.9±1.7
Hemoglobin	9.4±3.4	Creatinine	114.3±41.9
HCT	27.4±6.4	Amylase	45.4±29.9
WBC	7.8±6.4	Lipase	64.2±94.8
Platelet	72.9±30.8	Troponin T	302±252.9
INR	1.4±0.5	Myoglobin	4730±4318
PT	14.6±4.9	Bilirubin	28±17.8
APTT	55±36.3	ALT	54(13-1133)
Fibrinogen	1.6±0.9	AST	105(22-851)
pH	7.2±0.2	ALP	50.9±20.1
PO2	182.2±125.8	Lactate	8.2±5.4
PCO2	51.6±50	Mg	0.7±0.2
BE	-8.5±6.8	**ICU LOS**	5(1-75)
HCO3	18.3±5.9	**Hospital LOS**	3 (1-255)
Corrected Ca	2±0.3	ISS (mean±SD)	29.9±10.8
Ionised Ca	0.9±0.2	**RTS**	5.4±2.1
Sodium	146±12.2	Temp in ED	36.2±0.6
Potassium	4.4±0.8		
BUN	5.4 (3-61)		