Risk Stratification of Surgical Intensive Care Unit Patients based upon obesity: A Prospective Cohort Study

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Burden of Obesity

- Considered to be a global epidemic
  - Swinburn BA et al. The global obesity pandemic: shaped by global drivers and local environments. Lancet. 2011
- Overall global Burden of obesity:
  - 25% are overweight and 10% are obese.
    - Kelly T et al. Global burden of obesity in 2005 and projections to 2030. Int J Obes. 2008.
- One in every four individuals is either overweight or obese in Pakistan
  - Jafar TH et al. Prevalence of overweight and obesity and their association with hypertension and diabetes mellitus in an Indo-Asian population. CMAJ. 2006

Background and Rationale

- Adverse Consequences of Obesity:
  - Cardiometabolic Risk Factors
    - Hypertension
    - Diabetes
    - Hypercholesterolemia
  - Malignancies
    - Wang YC et al. Lancet. 2011
    - Xu T et al. 2014.
- Fat stores as valuable body reserves from Evolutionary perspective:
  - Famines
  - Physical Exertions
  - Injuries
    - Lev-Ran A. Diabetes Metab Res Rev. 2001.
    - Bellisari A. Obes Rev. 2008.

- Critically Ill Obese Patients:
  - Theoretically at advantage due to body reserves
- No conclusive evidence from available literature
  - Retrospective studies
  - Secondary analysis
    - Gupta R et al. J Parenter Enteral Nutr. 2013.
    - Hutagalung R et al. Intensive Care Med. 2011.
- Rationale
  - Risk Stratification,
  - Decision Making
  - Prognosis Counselling

Obesity Measurements

- Body Mass Index:
  - Weight in KG / (Height in meters) ^{2}
  - WHO definitions for Asian Population
    - Underweight — BMI <18.5 kg/m2
    - Normal weight — BMI ≥18.5 to 23 kg/m^2
    - Overweight — BMI ≥23.0 to 27.5 kg/m^2
    - Obesity — BMI ≥27.5 kg/m^2

- WHO Expert Consultation. Appropriate Body-mass Index For Asian Populations And Its Implications For Policy And Intervention Strategies. Lancet. 2004

- Waist Circumference:
  - Reliable tool as a measure of obesity
    - >90 cm for Males
    - >85 cm for Females

- Kartheuser AH et al. Annals of Surgery. 2013.
- Pratyush DD et al. Indian J endocrinol metab. 2012

Study Question and Objectives

- Research Question:
  - Is mortality rate of obese Surgical ICU patients different from mortality rate of non obese Surgical ICU patients?
- Primary Objective:
  - To measure impact of obesity upon mortality rate of surgical intensive care unit patients.
- Secondary Objectives:
  - To measure impact of obesity upon length of ICU stay of surgical intensive care unit patients.

Hypothesis

- Null Hypothesis:
  - Mortality rate of obese surgical ICU patients is not different from mortality rate of non obese surgical ICU patients.

- Alternate Hypothesis:
  - Mortality rate of obese surgical ICU patients is different from mortality rate of non obese surgical ICU patients.

Study Design

- Prospective Cohort Study:
  - Non-Exposed Cohort:
    - Waist Circumference < 90 cm for males / < 85 cm for females
    - BMI < 27.5 Kg/m^2
  - Exposed Cohort:
    - Waist Circumference $\geq$ 90 cm for males / $\geq$ 85 cm for females
    - BMI $\geq$ 27.5 Kg/m^2
      - Calculated form Weight and Height recorded at time of admission or best estimate in consultation with immediate family member

Population

- Target Population:
  - Adult Critically Ill Patients in Surgical ICU
- Study Population:
  - Adult Critically Ill Patients admitted in Surgical ICU of Aga Khan University Hospital Karachi
- Study Sample:
  - Those adult critically ill patients admitted in Surgical ICU of Aga Khan University hospital Karachi who fulfill eligibility criteria and give consent to participate.

Selection Criteria

- Patients Admitted in Intensive Care Unit
  - Age $\geq$ 16 Years
  - Both males and females
  - First Time Admission

- Exclusion Criteria:
  - Malignancy
  - Chronic Liver Disease with Ascites
  - ICU Stay < 24 Hours
  - Shifted out of Hospital
  - Direct Transfer to ICU from outside hospital

Sample Size

- WHO Software
  - Level of Significane 5%
  - Power 80%
- For Primary Outcome (Mortality):
  - Known Mortality in ICU 30%
  - Sample size to detect 15% difference 122
- For Secondary Outcome (Length of ICU Stay)
  - Known length of ICU Stay 11 +/- 14.2 Days
  - Sample Size to detect 5.5 Days Difference 105
- Considering 10% Loss to Follow up
- Required minimum sample size in each group = 122 + 10 = 132

- Goldhill DR et al. Outcome of intensive care patients in a group of British intensive care units. Crit Care Med. 1998.
- Pieracci FM et al. The relationship between body mass index and postoperative mortality from critical illness. Obes Surg. 2008

Sampling Technique and Settings

- Non-probability
  - Consecutive
- Study Setting
  - Hospital Based Study
- Study Site
  - Aga Khan University and Hospital
  - Surgical Intensive Care Unit
    - 12 bed ICU
    - Intensivist (Anesthesiologist)
      - Surgical Consultant

Outcome Measures

- Primary Outcome:
  - Mortality: During index hospital admission

- Secondary Outcome:
  - Length of ICU stay: Number of days from admission to ICU, to day of shifting out of ICU

Main Exposure of Interest

- Waist Circumference:
  - Within 24 hour of admission to ICU
  - At level of Iliac Crest
  - Cut off of ≥ 90 cm for males and ≥ 85 cm for females for asian population
    - Kartheuser AH et al. Annals of Surgery. 2013.
    - Pratyush DD et al. Indian J endocrinol metab
- Body Mass Index (BMI):
  - Weight and height recorded at time of admission
    - Weight in KG
    - Height in cm from vertex to heel
  - WHO cut off of ≥ 27.5 to define obesity
    - WHO Expert Consultation. Appropriate Body-mass Index For Asian Populations And Its Implications For Policy And Intervention Strategies. Lancet. 2004
  - Logistic issues especially for bed bound emergency patients

Other Risk Factors

- Socio-demographics:
  - Age
    - Hospital Medical Records
    - Numberm of Years
  - Gender
- Type of Admission:
  - Elective
  - Emergency

Other Risk Factors Cont…

- Co-Morbid Conditions:
  - Diabetes Mellitus
    - Ever diagnosed by physician
  - Hypertension:
    - Ever Diagnosed by physician
  - Ischemic Heart Disease:
    - Evidence of Angina or MI
  - Smoking Status

- Nature of Primary Diagnosis:
  - Infectious
  - Inflammatory
  - Trauma
  - Others

APACHE II Score

Physiologic Variable	High Abnormal Range					Low Abnormal Range				
	+4	+3	+2	+1	0	+1	+2	+3	+4	Points
Temperature - rectal (°C)	≥41°	39 to 40.9°		38.5 to 38.9°	36 to 38.4°	34 to 35.9°	32 to 33.9°	30 to 31.9°	≤29.9°	
Mean Arterial Pressure - mm Hg	≥160	130 to 159	110 to 129		70 to 109		50 to 69		≤49	
Heart Rate (ventricular response)	≥180	140 to 179	110 to 139		70 to 109		55 to 69	40 to 54	≤39	
Respiratory Rate (non-ventilated or ventilated)	≥50	35 to 49		25 to 34	12 to 24	10 to 11	6 to 9		≤5	
Oxygenation: A-aDO2 **or** PaO2 (mm Hg) a. FIO2 ≥0.5 record A-aDO2 b. FIO2 <0.5 record PaO2	≥500	350 to 499	200 to 349		<200 PO2>70	 PO2 61 to 70		 PO2 55 to 60	 PO2<55	
Arterial pH (preferred) Serum HCO3 (venous mEq/l) (not preferred, but may use if no ABGs)	≥7.7 ≥52	7.6 to 7.69 41 to 51.9		7.5 to 7.59 32 to 40.9	7.33 to 7.49 22 to 31.9		7.25 to 7.32 18 to 21.9	7.15 to 7.24 15 to 17.9	<7.15 <15	
Serum Sodium (mEq/l)	≥180	160 to 179	155 to 159	150 to 154	130 to 149		120 to 129	111 to 119	≤110	
Serum Potassium (mEq/l)	≥7	6 to 6.9		5.5 to 5.9	3.5 to 5.4	3 to 3.4	2.5 to 2.9		<2.5	
Serum Creatinine (mg/dl) Double point score for acute renal failure	≥3.5	2 to 3.4	1.5 to 1.9		0.6 to 1.4		<0.6			
Hematocrit (%)	≥60		50 to 59.9	46 to 49.9	30 to 45.9		20 to 29.9		<20	
White Blood Count (total/mm3) (in 1000s)	≥40		20 to 39.9	15 to 19.9	3 to 14.9		1 to 2.9		<1	
Glasgow Coma Score (GCS) Score = 15 minus actual GCS										
A. Total Acute Physiology Score (sum of 12 above points)										
B. Age points (years) ≤44=0; 45 to 54=2; 55 to 64=3; 65 to 74=5; ≥75=6										
C. Chronic Health Points (see below)										
Total APACHE II Score (add together the points from A+B+C)										

Data Collection Methods

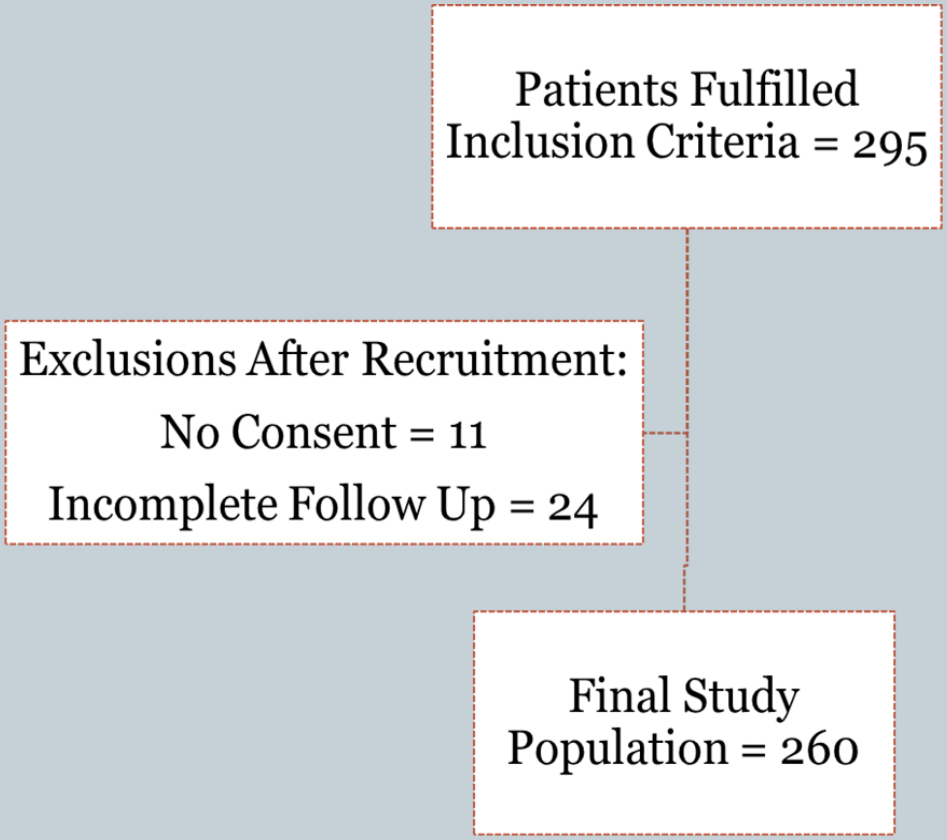
- Waist Circumference was measure within 24 hours of admission to ICU at level of iliac crest.
- Parameters to calculate for APACHE II Score were measured in initial 24 hours after admission.
  - Continuous Scale

Ethical Cosiderations

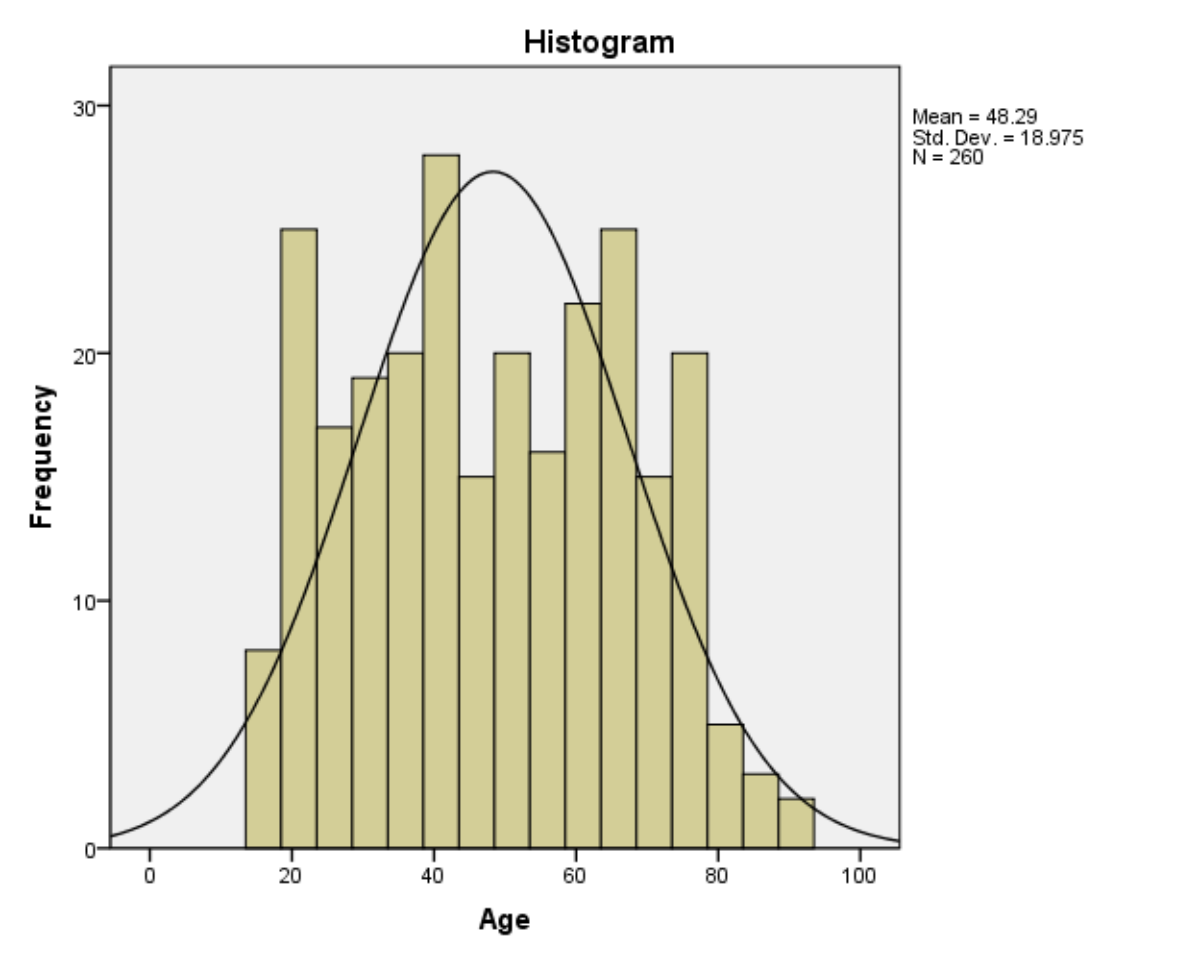
- Vulnerable Population
  - Patients clinical needs always given priority
- Informed Consent Form
  - In Urdu Language as well
  - Understanding of nature of study made sure before consenting
  - 1st degree relative in case patient was not in state of mind to understand nature of study.
- ERC Approval Sought: 3233-CHS-ERC-14

Results

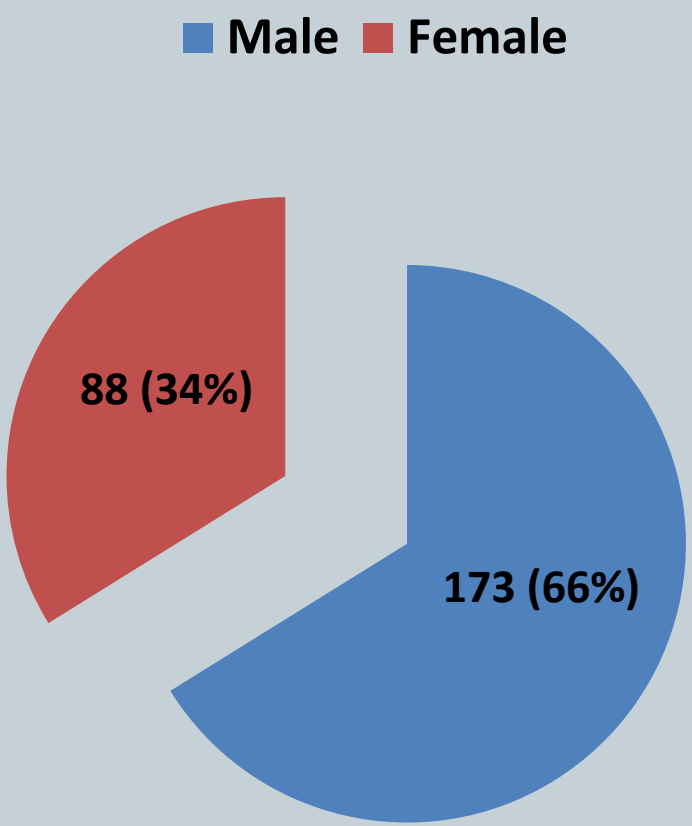
- Aug 01, 2014 to March 15, 2016



Age

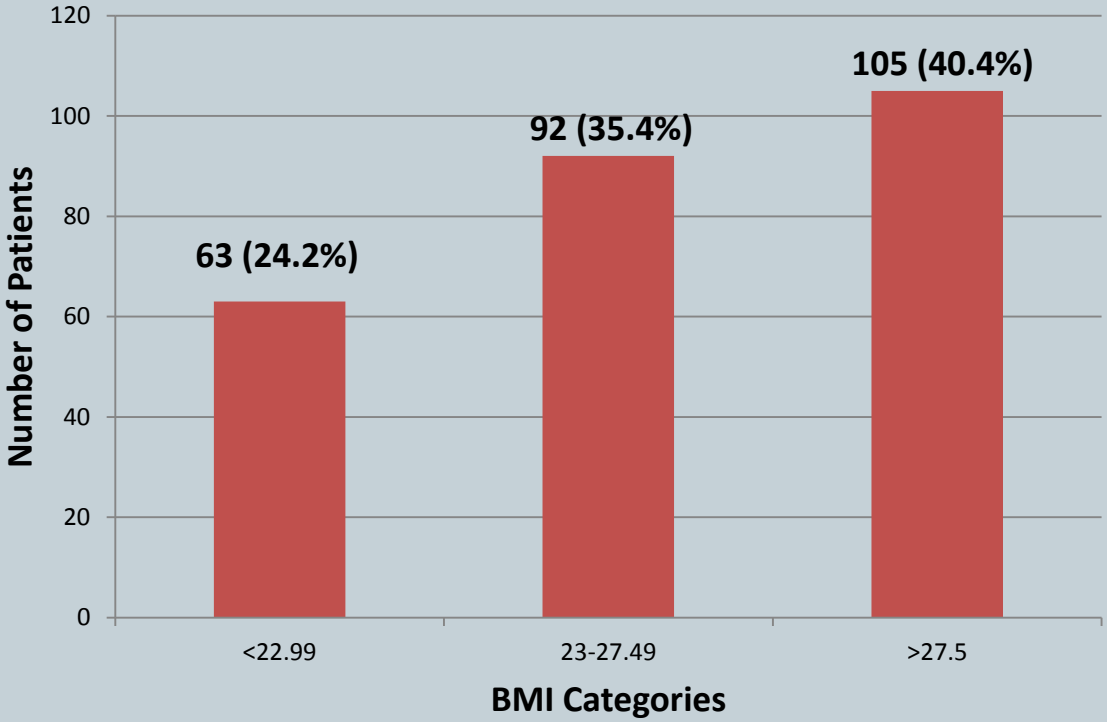

Histogram
Mean = 48.29
Std. Dev. = 18.975
N = 260
Frequency
30
20
10
0
0
20
40
60
80
100
Age

Gender



Obesity

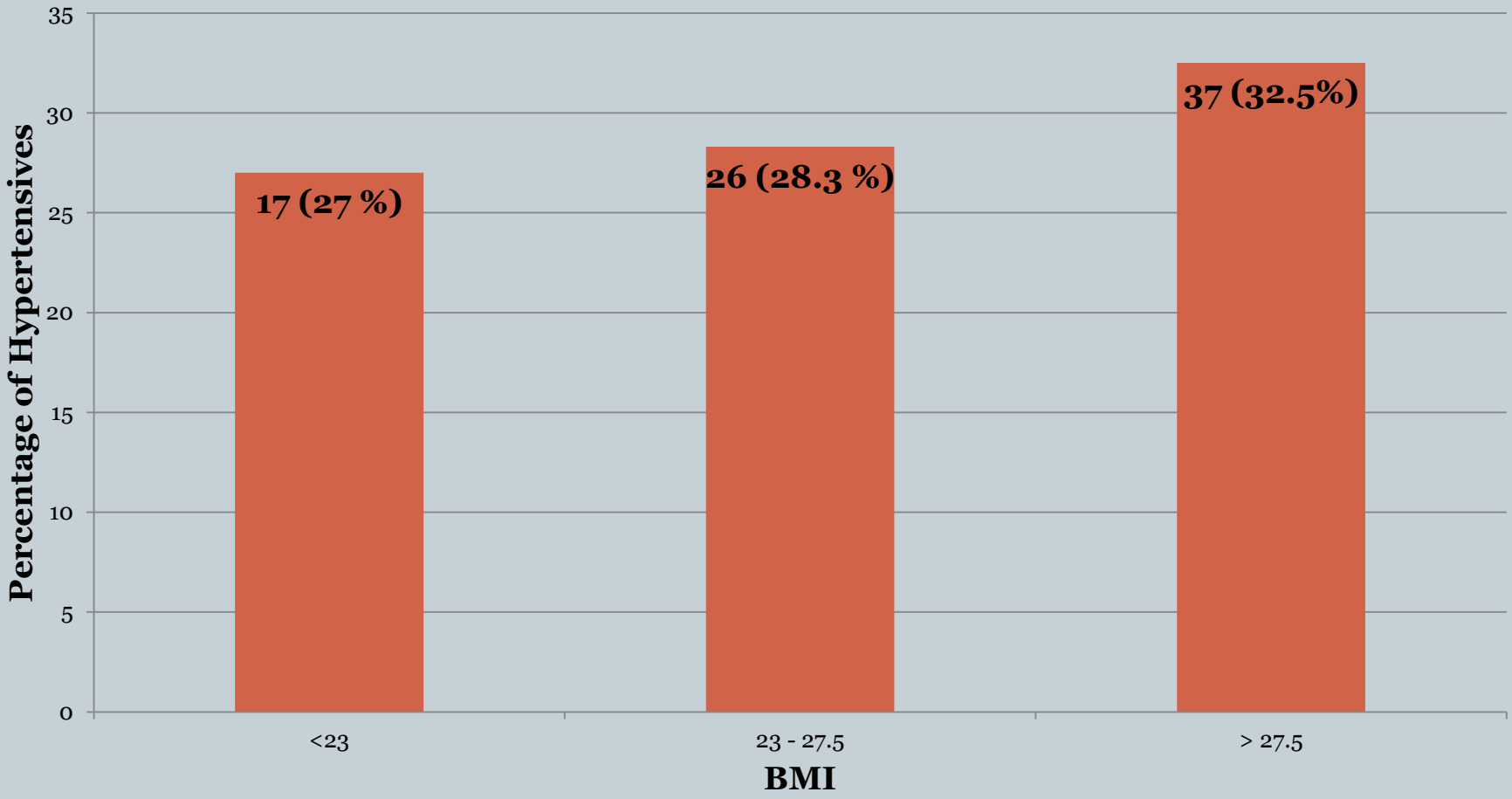
- As measured by waist circumference: 237 (91.2%)
- As measure by BMI



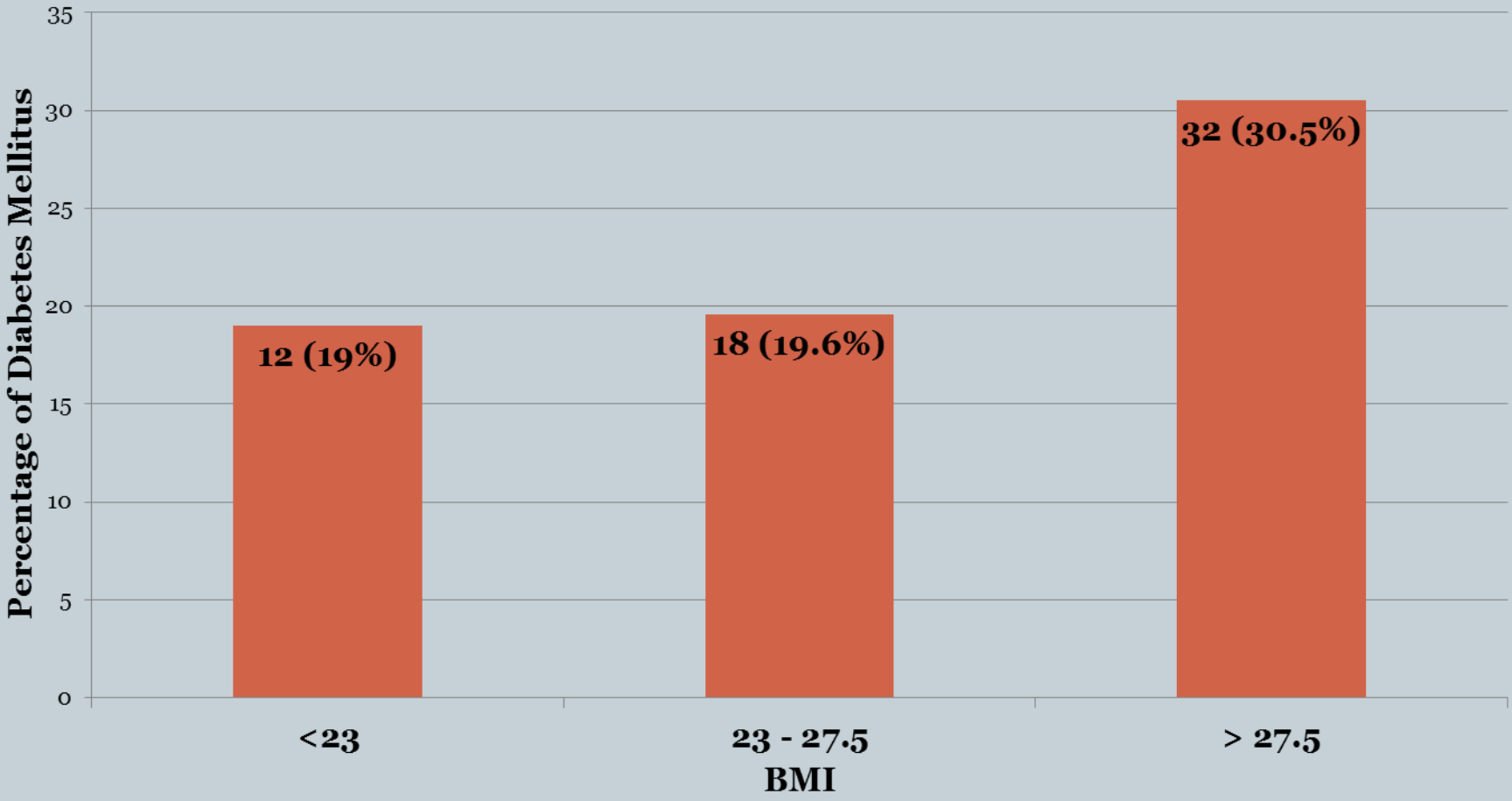
Co – Morbid Conditions

Variable	Measurement	Number	Percentage
Diabetes Mellitus	Present	62	23.8
Hypertension	Present	80	30.8
Ischemic Heart Disease	Present	32	12.3
Emergency Admission	Yes	235	90.4
Smoking	Current	13	5
	Past	42	16.2
	Never	205	78.8
Nature of Disease	Infectious	100	38.5
	Inflammatory	41	15.8
	Trauma	72	27.7
	Others	47	18.1

Hypertension



Diabetes Mellitus



Co – Morbid Conditions

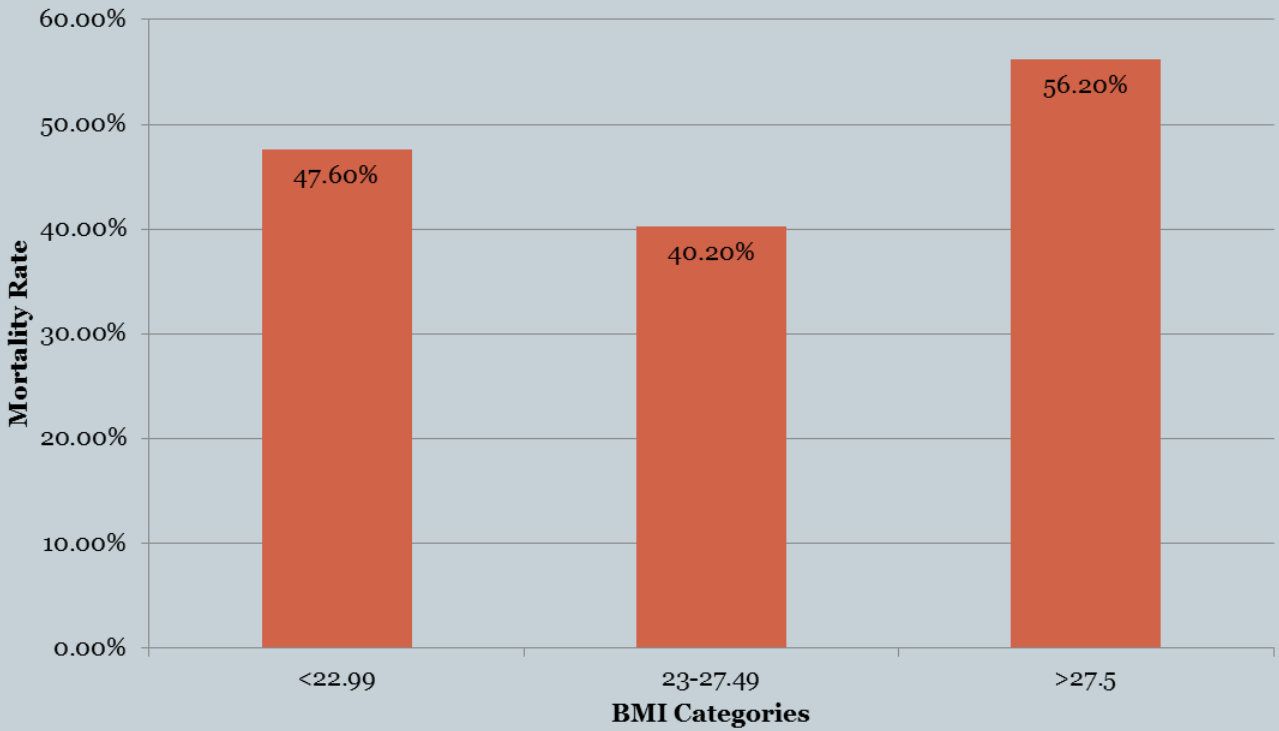
BMI	BMI <23	BMI 23 – 27.5	BMI > 27.5
Ischemic Heart Disease	8 (12.5%)	12 (13%)	12 (11.4%)
Emergency Admission	52 (82.5%)	85 (92.4%)	98 (93.3%)

- Overall Mortality: 126 (48.5%)
- Length of ICU Stay:
  - Mean +/- SD: 11.86 +/- 8.95
- APACHE II Score:
  - Mean +/- SD: 14.21 +/- 10.86

Univariable Analysis (Mortality)

Variable	Reference Category	Relative Risk	P Value	Log Likelihood
Waist Circumference	Non obese	.92	0.709	-180.02559
Mid-Arm Circumference	Non obese	1.07	0.571	-179.93443
BMI	**Non obese**	**1.29**	**0.041**	**-177.98447**
Age		**1.02**	**0.001**	**-174.69807**
Gender	Male	.97	0.865	-180.08081
H/O DM	No	.85	0.264	-178.8051
H/O HTN	**No**	**.74**	**0.028**	**-177.63912**
H/O IHD	No	.79	0.190	-179.22233
Emergency Admission / Operation	No	1.08	0.710	-180.02588
APACHE II Score		**1.03**	**0.000**	**-170.35695**

Mrotality for 3 BMI Categories



- P Vale = .081

Multivariable Analysis (Mortality)

New Variable	Variables in Model	Name of Model	B_i	P value of B_i	P Vale (Overal Model)	LL of Model	LR Test Statistic (p Value)	Decision
Waist Circumference	Waist Circumference	Model1	.92	0.709	0.709	-180.02		
APACHE Score	**Waist APACHE**	**Model2**	**.86 1.02**	**0.62 0.002**	**<0.006**	**-154.41**	**1 Vs 2 19.65 (<0.001)**	**Keep APACHE in Model**
Age	Waist APACHE Age	Model3	0.84 1.02 1.01	0.681 0.009 0.12	0.005	-152.00	2 Vs 3 2.82 (0.132)	Remove Age from Model
HTN	Waist APACHE HTN	Model4	0.88 1.02 0.75	0.681 0.002 0.123	0.006	-150.74	2 Vs 4 1.34 (0.247)	Remove HTN From Model
BMI	**Waist APACHE BMI**	**Model 5**	**0.75 1.02 1.4**	**0.75 0.002 0.048**	**0.003**	**-130.21**	**2 Vs 5 10.52 (0.02)**	**Keep BMI in Model**

Univariable Analysis (ICU Length of Stay)

Variable	Slope Co-efficient	MSE	R^2	F-test	p-value
Waist Circumference	.0449521	.042348697	0.0000	0.00	0.968
BMI	.9472705	55.8487263	0.0083	2.15	0.244
Mid-Arm Circumference	-.0893116	.510007134	0.0001	0.02	0.889
Age	.0220389	45.2930117	0.0067	1.74	0.288
Gender	-.1091839	.692622476	0.0001	0.03	0.871
H/O DM	5.532258	44.3095609	0.0132	1.71	0.282
H/O HTN	1.22095	82.4211773	0.0122	3.19	0.075
H/O IHD	2.873899	231.642891	0.0344	9.16	0.003
Emergency Admission / Operation	-.3916239	3.46413292	0.0005	0.13	0.716
APACHE II Score	.0026287	.209713519	0.0000	0.01	0.929

Variables in Model	Adj R^2	Overall F-test	p-value	MSE	New Variable p-value
Waist Circumference, IHD	**0.0270**	**4.58**	**0.011**	**116.257**	**0.003**
Waist Circumference, IHD, HTN	0.024	3.12	0.026	79.335	0.64

Discussion

- <u>Similar Outcome:</u>
- Outcome of 13000 intensive care unit admission patients over a period of five year
- Being overweight or obese was associated with decreased 60-days in hospital mortality.

- Hutagalung, r., Et al., The obesity paradox in surgical intensive care unit patients. Intensive care medicine. 37(11): p. 1793-1799.

- BMI was determinant of short to medium term survival.
- Obesity was not associated with increased morbidity and could be protective for critically ill patients.

- Peake, S.L., Et al., The effect of obesity on 12-month survival following admission to intensive care: A prospective study*. Critical care medicine, 2012. 34(12): p. 2929-2939.

- A few retrospective studies and secondary analysis of data have reported no difference in mortality of critically ill patients

  - Pieracci, F.M., Et al., The relationship between body mass index and postoperative mortality from critical illness. Obesity surgery, 2008. 18(5): p. 501-507.
  - Sakr, y., Et al., Obesity was associated with increased morbidity but not mortality in critically ill patients. Intensive care medicine, 2008. 34(11): p. 1999-2009.

- Severe obesity was significantly associated with adverse outcomes and increased resource utilization in **trauma patients** treated admitted to ICU.
  - Duchesne, J.C., Et al., Impact of obesity in damage control laparotomy patients. Journal of trauma-injury, infection, and critical care, 2009. 67(1): p. 108-114.

- <u>Meta-analysis:</u>
- Fourteen studies having about sixty two thousand patients collectively.
- They found that obesity in critically ill patients is not associated with excess mortality
- significantly related to prolonged duration of mechanical ventilation and intensive care unit length of stay.
  - Hogue jr, C.W., Et al., The impact of obesity on outcomes after critical illness: a meta-analysis. Intensive care medicine, 2013. 35(7): p. 1152-1170.

Conclusion

- Risk of mortality for Obese patients as measure by BMI ≥27.5 is 1.4 times greater than non-obese patients (BMI <27.5), adjusting for critical illness and comorbids.
- Non significant trend of mortality rate of overweight patients being less than Normal or Obese patients
- Waist Circumference is not good measure of obesity in ICU, probably due to tissue oedema and other factors.

Strengths

- First Ever Prospective Study
- Adjustment for critical illness

Limitations

- Single Centre
- Precise measurements of weight not possible

Thank You