To determine the non-invasive investigations which correlate with liver biopsy in extent of fibrosis in morbidly obese patients undergoing bariatric surgery

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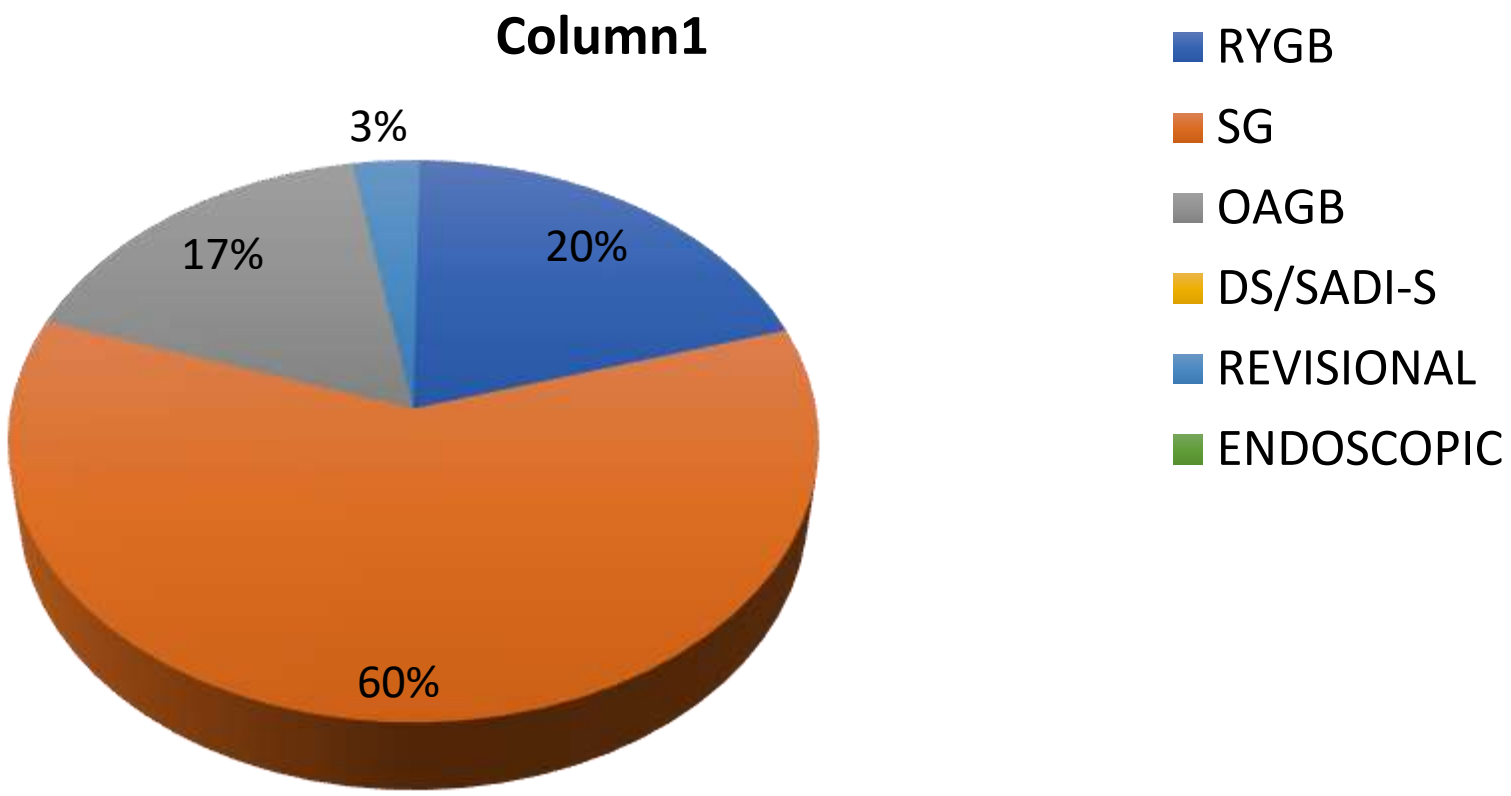
I have no potential conflict of interest to report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Background

- Prevalence of NAFLD in morbidly obese individuals in India 67.5%-%-79.4%
- Preoperative Detection of Fibrosis(F3,4) in Patients undergoing Bariatric Surgery is important-
  - Increased Risk of Perioperative Complications
  - continuous monitoring for progression/ Response to Treatment
- Liver Biopsy: Invasive; Sampling Error
- Ongoing Search for Tools for Non-invasive fibrosis Detection to avoid unnecessary Biopsies

Praveen Raj et al. Obes Surg 2014
Garg H, et al SOARD 2017 .

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Aims & Objectives

- **Aim:** Evaluate various non-invasive investigations to predict fibrosis in morbidly obese patients by correlating with liver biopsy
- **Primary Objective:** Determine the non-invasive marker which correlates the most with the liver biopsy in the extent of fibrosis in morbidly obese patients undergoing bariatric surgery

Non –Invasive Tests

Test	Components
Transient Elastography (TE)	LSM and CAP
FIB-4 Fibrosis Index	Age, AST, ALT, Platelet Count
APRI (AST to platelet ratio index)	AST, Platelets
ELF (Enhanced Liver Fibrosis)	Hyaluronic acid (HA), Procollagen III amino terminal peptide (PIIINP), Tissue inhibitor of metalloproteinase 1 (TIMP-1)

Methodology

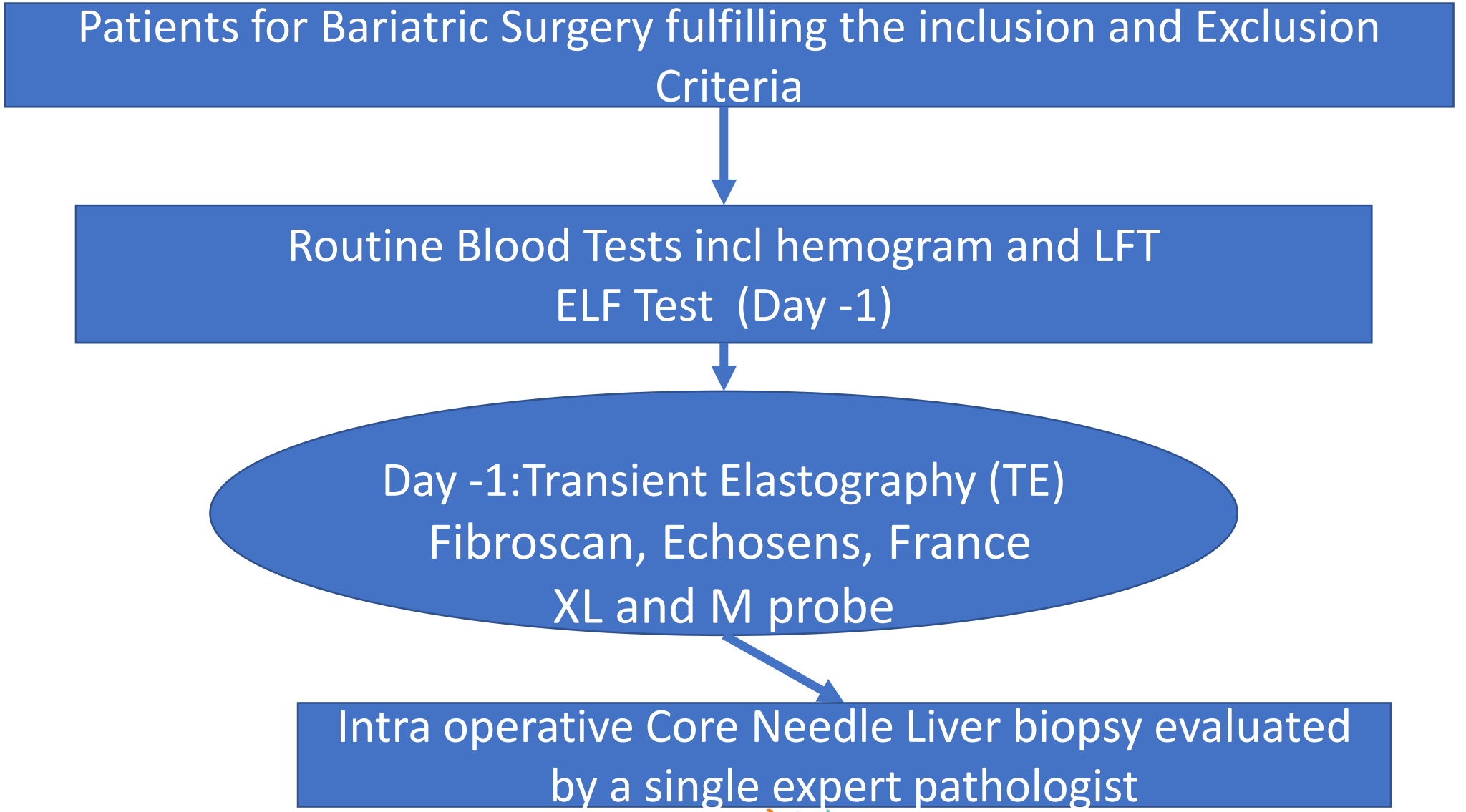
- **Setting:** Department of Surgical Disciplines, AIIMS, New Delhi
- **Study period:** March 2020 – November 2021 (Prospective study)
- Approved by the local ethics committee ; Written Informed Consent

Inclusion Criteria

- BMI ≥ 37.5kg/m^2 or ≥ 32.5 kg/m^2 + comorbidities
- 18-65 years of age

Exclusion Criteria

- Alcohol consumption > 20 gm/day
- Hepatitis B or Hepatitis C infection
- Auto-immune disease/ Metabolic storage disorder ; Certain Drugs including Steroids


Patients for Bariatric Surgery fulfilling the inclusion and Exclusion Criteria
Routine Blood Tests incl hemogram and LFT
ELF Test (Day -1)
Day -1:Transient Elastography (TE)
Fibroscan, Echosens, France
XL and M probe
Intra operative Core Needle Liver biopsy evaluated by a single expert pathologist

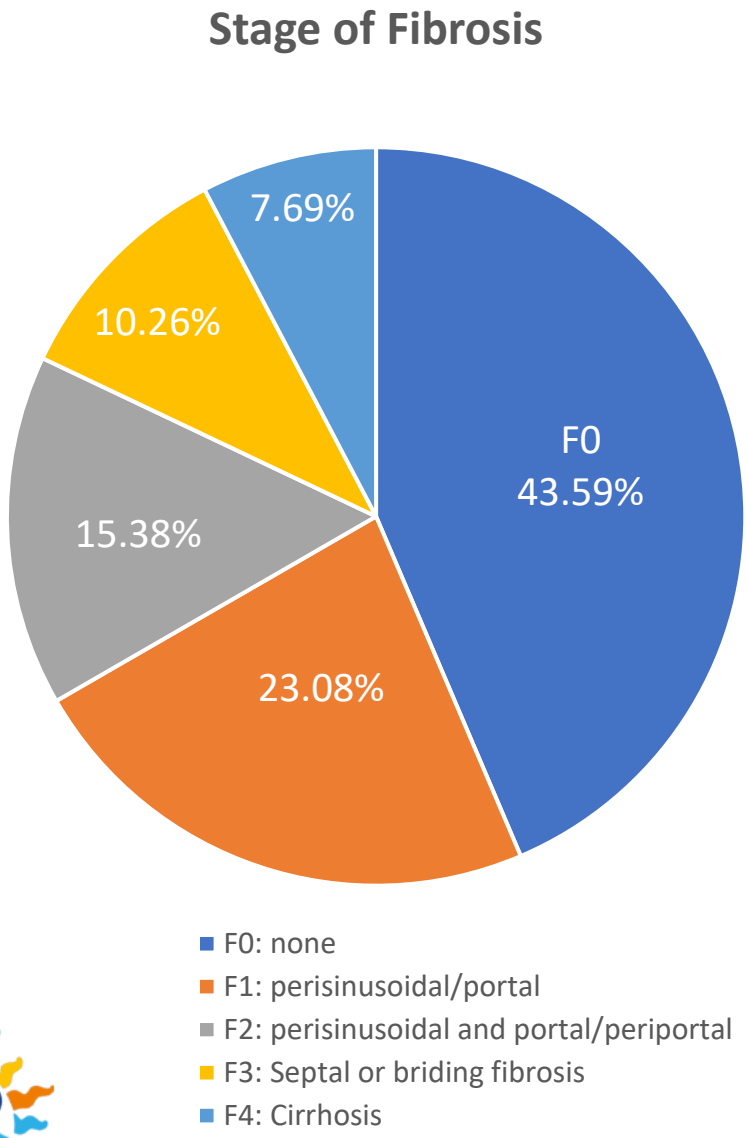
Baseline characteristics (n=48)

Characteristic	Value
Age	40.5 ± 12.8
Females, n (%)	34 (71%)
Body Mass Index (kg/m^2)	44.4 ± 7.8
Diabetes Mellitus n (%)	15 (31.2%) [HbA1c: 5.9]
Total bilirubin mg/Dl	0.46 (0.31-0.54)
Alanine Transaminase, ALT IU/L	**25.5 (19-37.75)**
Aspartate Transaminase, AST IU/L	**27.5 (23-37.2)**
Alkaline Phosphatase, ALP IU/L	98.5 (82.7-113.7)

Baseline Liver biopsy (n=41)

- Prevalence of NASH (NAS 5 or more)- 10.8%

- F0-F1 66.6%
- F2 or More 33.3 %
- F3 or more 17.9%
- F4 7.6%



Liver biopsy Findings

	Normal LFTs	**Abnormal LFTs**	**p-value**
Steatosis (S ≥2)	33.3%	66.67%	0.006
NASH	50%	50%	0.58
Significant Fibrosis (F≥ 2)	38.46%	61.5%	0.03

No correlation was seen between degree of histologic liver damage and presence of diabetes

Non-invasive tests

Sno	Name	No. of Observations	Median	IQR
1	LSM	46	8	6.7-13.9
2	CAP	46	333	291-362
3	ELF	45	8.76	8.07-9.46
4	APRI	48	0.33	0.24-0.57
5.	Fib4	48	0.8	0.63-1.2

Accuracy of Non Invasive Tests

Test	AUROC	Significant Fibrosis (F2 to F4)					AUROC	Advanced Fibrosis(F3 to F4)				
		Cut off	Se(%)	Sp(%)	PPV (%)	NPV (%)		Cut off	Se(%)	Sp(%)	PPV (%)	NPV (%)
LSM	0.75	7.5	91.6	57.6	50	93.8	0.80	9.2	83.3	71.9	35.7	95.6
ELF	0.80	9.1	84.6	78.2	68.8	90	0.85	9.33	85.7	82.8	54.5	96
APRI	0.70	0.5	61.5	80.7	61.5	80.8	0.76	0.6	71.4	84.4	50	93.1
FIB4	0.55	0.84	61.5	53.8	40	73.7	0.59	1.07	57.1	75.0	33.3	88.9

- ELF: Best marker to predict Significant and Advanced Fibrosis (Sensitivity of 84.6% and 85.7% at cut offs of 9.1 and 9.33 respectively)
- LSM: best marker to predict any degree Fibrosis (Cut off of 6.7 and sensitivity of 95%)
- FIB 4 has poor correlation with Liver biopsy and thus is not useful
- APRI can be used if ELF and TE are not available
- All the non-invasive markers have high NPV-more helpful in ruling out Fibrosis.

Many studies on TE in Obese patients undergoing Bariatric Surgery

- Barsamian et al- AUROC of 0.7, 0.83 and 0.89 for any Fibrosis, SF and AF). Cut off's were 7, 8.1, 8.7kPa respectively
- Eddowes et al- AUROC of 0.8 for AF at cut-off 9.7kPa
- Karlas et al reported poor performance of TE in bariatric patients

Karlas T et al. Plos ONE 2015

Barsamian C et al. Clin Nutr ESPEN 2020

Eddowes PJ et al. Gastroenterology 2019

- Paucity of Studies on use of ELF in Patients Undergoing Bariatric Surgery

- Karlas et al: ELF score correctly classified 87.5% of patients with any fibrosis
    - *Only 1 patient had F3*
    - *cut-off for significant fibrosis was transferred from a non-bariatric cohort*

- Inadomi et al.-AUROC of 0.8 for Significant Fibrosis; cut off obtained was 9.86.;
  However Median BMI was only 28.6kg/m2
- An ELF cut-off point of 8.72 allows the detection of patients with NASH with a sensitivity of 71.4% and a specificity of 74.1% (AUC = 0.742, p = 0.002)

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Inadomi C et al. Hepatol Res 2020

Karlas T et al. Plos ONE 2015

Lopez IC etal. Obes Surg 2017

Strengths and Limitations

Strengths

- Direct comparison of ELF score, APRI, FIB-4, and LSM in the same patients
- Assessment of liver histology by a single experienced hepatopathologist
- Providing optimized cut-offs for ELF, and LSM, CAP

Limitations

- Lack of internal validation of our findings
- Relatively small number of 48 obese patients included
- Selection bias, as all participants included were those who underwent bariatric surgery

Thank you