




# Ultrasound Shear Wave Elastography of Normal Pancreas in Adult Subjects

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## Abstract

**Background and Purpose** Transabdominal ultrasound (US)-based shear wave elastography (SWE) provides an attractive method of estimating pancreatic stiffness. There is limited data on the SWE values of the healthy pancreas in Indian subjects. The current study aimed to evaluate SWE of the normal pancreas.

**Methods** We performed a study from January 2019 to March 2019. We included adult patients who presented for the US of the upper abdomen for vague abdominal symptoms, unrelated to the pancreas. The SWE values were obtained from the pancreatic head and body. The association of pancreatic SWE with age, gender, fatty liver, chronic liver disease, and cholelithiasis was recorded.

**Results** During the study period, 205 subjects underwent SWE of the pancreas. The mean age of subjects was 41.3 (standard deviation [SD] 15.3) years. There were 93 males and 112 females. The mean SWE value in the head of the pancreas was 8.98 (SD 2.46 kPa), and that in the body region was 8.67 (SD 2.67 kPa). There was a positive correlation of SWE with age. The SWE of the pancreatic body was significantly higher in patients who had a fatty liver on US ( $p < 0.05$ ). There was no significant association of SWE of the pancreas with gender, presence of chronic liver disease, or gallstones.

**Conclusion** The normal values of pancreatic SWE are correlated with age and fatty change in the liver.

## Keywords

- ▶ pancreas
- ▶ stiffness
- ▶ shear wave elastography

## Introduction

Pancreas is affected by various focal and diffuse diseases. Changes in the pancreatic stiffness can occur because of various physiological processes such as aging, diabetes, body mass index (BMI), and inflammatory conditions. The commonly employed diagnostic modalities for evaluation of pancreatic pathologies are ultrasound (US), computed tomography, magnetic resonance imaging (MRI), and endo-

scopic US (EUS).<sup>1</sup> However, these techniques are not able to evaluate the stiffness of the pancreas. Pancreatic stiffness can be an important indicator in the differentiation between malignant and benign pancreatic tumors, for detection of chronic pancreatitis, and for identifying high-risk patients for pancreatic cancer (familial pancreatic cancer or germline mutation with a lifetime cumulative risk of  $> 5\%$ ).<sup>2,3</sup> In surgical practice, evaluation of pancreatic stiffness may allow preoperative prediction of patients at high risk of

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development of postoperative pancreatic fistula following pancreaticoduodenectomy.<sup>4</sup>

Elastography is a noninvasive imaging technique to evaluate the stiffness of various organs. This technique has been used successfully for the evaluation of liver fibrosis, breast, and thyroid lesions.<sup>5-7</sup> For pancreas, elastography can be performed using US, EUS, or MRI.<sup>2</sup> The techniques of performing elastography on US include transient elastography, strain elastography, two-dimensional (2D) shear wave elastography (SWE) and point SWE (pSWE).<sup>2</sup> SWE is preferred over strain elastography as it is less operator-dependent. SWE relies on the principle of acoustic radiation force impulse (ARFI) using an US probe that then propagates through the tissue to be evaluated. The shear wave velocity (SWV) depends on the stiffness of the tissue.<sup>8,9</sup> Although there are some studies that provide normative values of pancreatic stiffness in western population<sup>10</sup> and in healthy children and adolescents,<sup>11</sup> there is limited data on the normative values of pancreatic stiffness in Indian population. It is important to be aware of the normal SWE values to apply this advanced imaging technique for identification of pancreatic pathologies. The current study aimed to investigate the SWE values of the normal pancreas.

## Methods

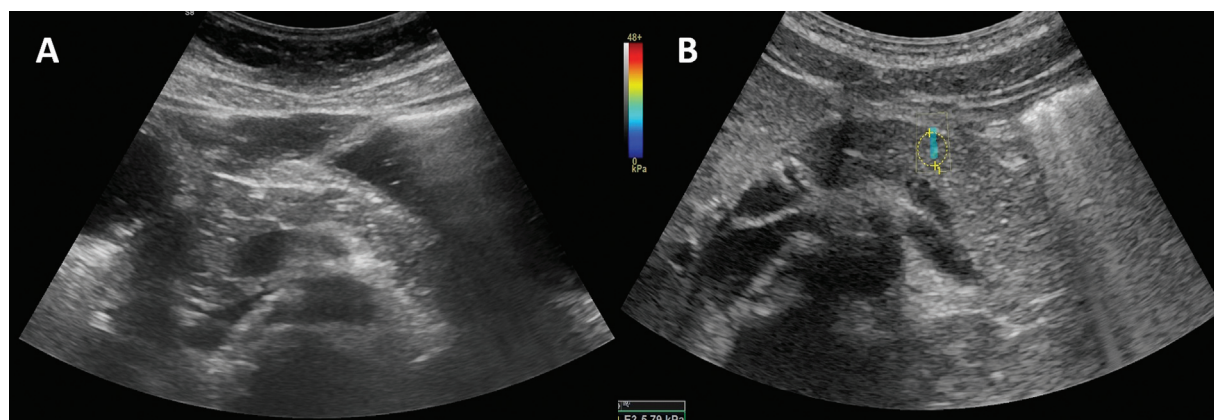
This was a cross-sectional study performed on a group of patients with BMI within the normal range who presented to a tertiary care referral center with vague abdominal complaints that were clinically deemed unrelated to pancreas. The study was performed between January 2019 and March 2019. Study was approved by the institutional ethics committee and the need to obtain consent was waived off. According to the revised consensus, the normal BMI for Indians is 18.5 to 22.9 kg/m<sup>2</sup>.<sup>12</sup> Patients with BMI outside the reference range, those with diabetes mellitus, or any pancreas-related symptoms (typical pancreatic pain or pancreatic diarrhea) as well as patients with a known diagnosis of pancreatic disease (acute or chronic pancreatitis, pancreatic or peripancreatic neoplasms) were

excluded. In addition, patients in whom SWE could not be performed due to bowel gases or poor breath hold were also excluded.

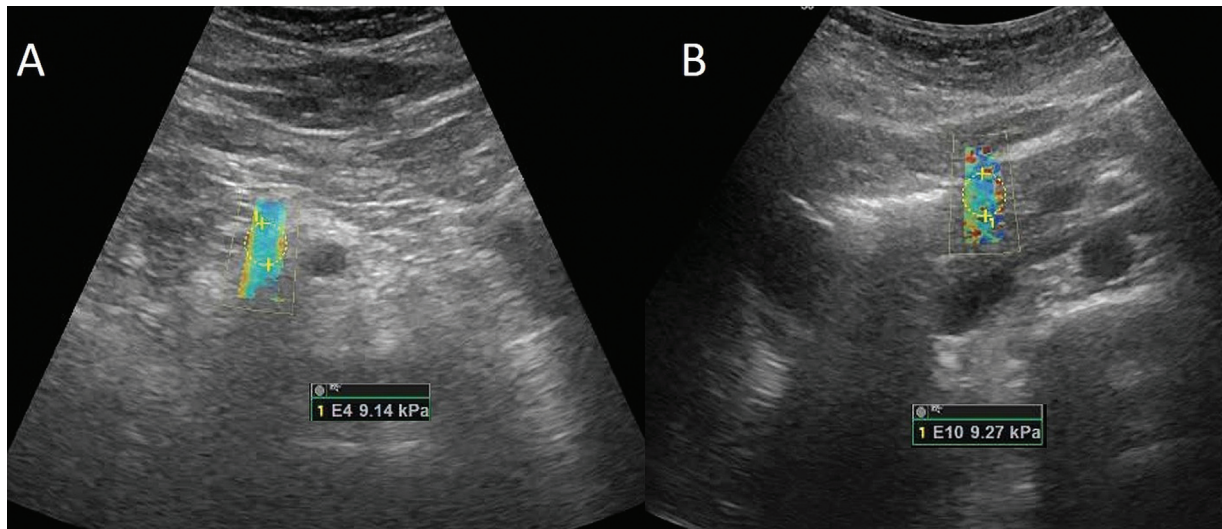
## The Technique of Shear Wave Elastography

Prior to performing SWE of pancreas, the two radiologists (S. C. and M.V.) were trained by the radiologist (P.G.) having 1 year of experience in performing liver and pancreatic SWE. Although a single radiologist performed SWE, the images were reviewed by the experienced radiologist (P.G.) for adequacy of measurements with respect to the correct placement of the region of interest (ROI). Patients were kept fasting for 6 to 8 hours before the procedure. The entire US (including SWE) was performed in a supine position with both hands placed overhead. US examinations were performed by one of the three radiologists with 4 to 8 years' experience in abdominal sonography. US was performed on a high-end system (Logic S8, GE Healthcare, United States) with the convex probe (3–5 MHz). The pancreas was initially evaluated on B-mode. If the pancreas was not clearly visualized, patients were instructed to drink 300 mL of water to provide a window for visualization of the pancreas. Pancreas which showed sonographically unremarkable morphology (slight hyperechoic, granular appearance, smooth, or slightly lobulated outline) were included in the study. Patients were trained to hold breath for 8 to 10 seconds during acquisition of the elastography values. SWE was performed in suspended respiration using the same transducer (convex probe 2–5 MHz). ROIs (0.5–1 cm<sup>2</sup>) for measurement of stiffness were placed on the segments of the pancreas, which were clearly visualized on grayscale US (►Fig. 1). Two measurements, each of head and body were taken (►Fig. 2). Mean of the two values at head and body was calculated. As the tail is not consistently seen in all the patients, values from the tail were not obtained. This was done to prevent motion-related errors. The total scan time was approximately 10 to 15 minutes. The value displayed on the machine was in kilopascal (kPa) which was subsequently converted to SWV in m/s using the formula:

$E = 3 \rho v^2$ , where  $E$  is the shear wave stiffness in kPa,  $\rho$  is the density of tissue (taken as 1), and  $v$  is the SWV.<sup>13</sup>



**Fig. 1** (A) Grayscale appearance of a normal pancreas. (B) Shear wave elastography measurement from the body.



**Fig. 2** Shear wave elastography in a patient with fatty liver. Stiffness of the pancreatic head (A, 9.14 kPa) was comparable to that of the body (B, 9.27 kPa).

The US assessment of liver (fatty liver and the presence of chronic liver disease [CLD]) and gallbladder was done. The diagnosis of CLD was based on comprehensive clinical and imaging criteria, including increased liver stiffness measurement by fibroscan. The correlation of the SWE values with age was done using the Spearman's correlation coefficient. The association of the SWE values with gender, fatty liver, CLD, and gallstones were tested using the chi-square test/Student's *t*-test/Mann-Whitney *U* test depending upon the normality of distribution (the normality of data was checked using Kolmogorov-Smirnov test). A *p*-value of < 0.05 was considered statistically significant.

## Results

Our study had a total of 205 subjects. There were 93 males and 112 females. The mean age of subjects was 41.3 (standard deviation [SD] 15.3) years (range, 18–78 years).

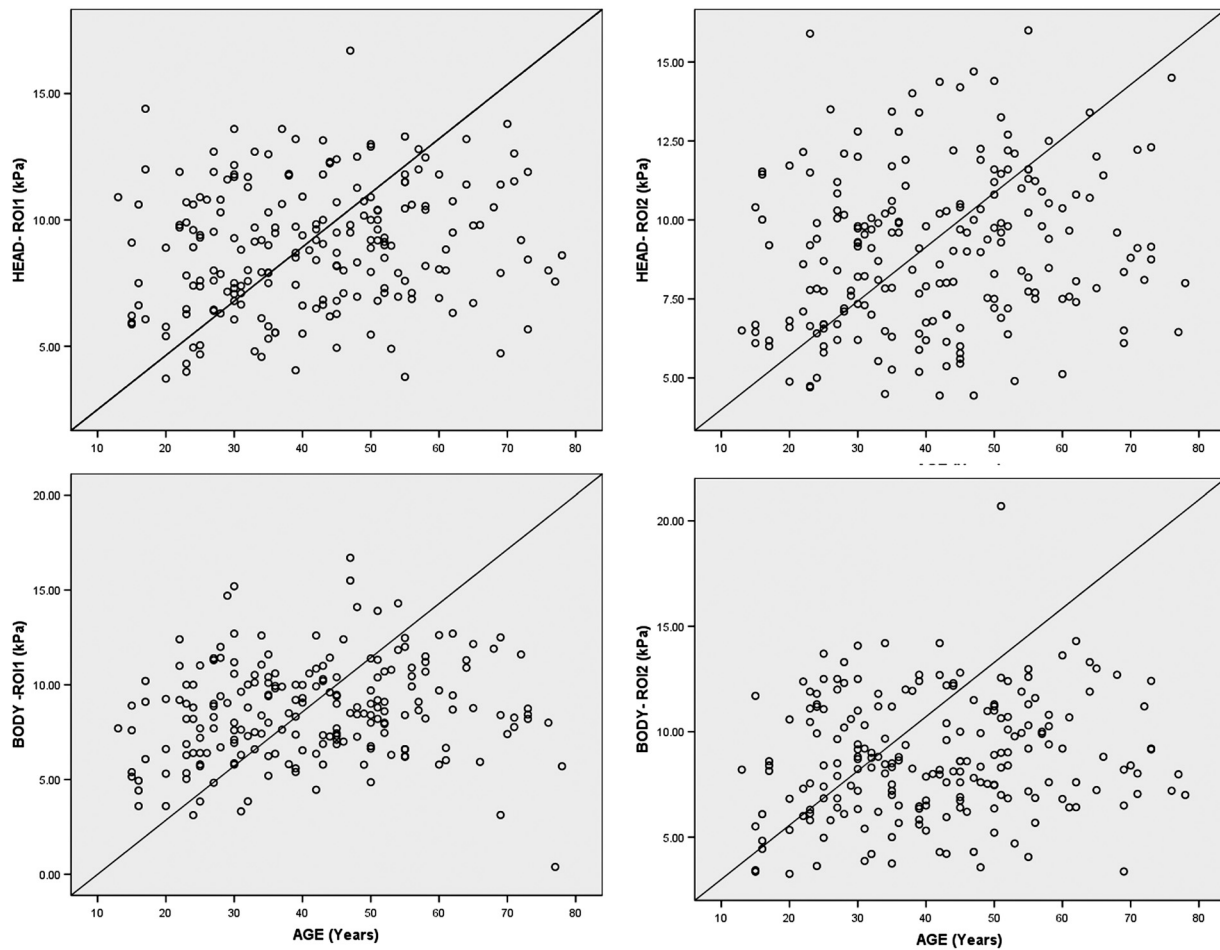
The mean SWE value in the head of the pancreas was 8.98 (SD 2.46 kPa) (ROI 1–8.93 kPa, ROI 2–9.03 kPa), and that in the body region was 8.67 (SD 2.67 kPa) (ROI 1–8.60 kPa, ROI 2–8.74). The values of SWV were 1.72 (SD 0.91) m/s in the head region and 1.70 (SD 0.94) m/s in the body region. The minimum value in the head of the pancreas was 3.72 kPa, and in the body region was 3.26 kPa. The maximum values in the head were 16.70 kPa and in the body were 20.70 kPa. There were no significant differences in the SWE values in the head and body of pancreas ( $p = 0.780$ , Mann-Whitney *U* test). There was a positive correlation of SWE with age (Spearman's correlation coefficient 0.142–0.201,  $p = 0.01$ ) (–Fig. 3, –Table 1). There was no significant difference in the SWE values based on gender ( $p = 0.641$ , Mann-Whitney *U* test). On grayscale US, 109 (53.2%) patients had normal US. Thirty-eight (18.5%) patients had fatty liver, 33 (16.1%) patients had CLD, and 25 (12.2%) patients had gallstone disease. The SWE values of the body of the pancreas were significantly higher in patients who had a fatty liver com-

pared with normal subjects ( $p = 0.02$ , Student's *t*-test); however, there was no association of SWE values with the grade of fatty liver. There was no significant difference in the SWE values of the pancreas in patients with CLD/gallstone disease versus normal subjects. –Table 2 shows the SWE values in different groups of patients.

## Discussion

We found that the normal pancreas has SWE values of 8.98 (SD 2.46) kPa and 8.67 (SD 2.67) kPa, in the head and body, respectively. Additionally, we found a positive correlation of SWE with age. SWE values were significantly higher in patients with fatty liver. However, we did not find any association between SWE values with CLD or gallstone disease.

Published data on SWE values in pancreatitis, pancreatic tumors, cystic fibrosis, and type 1 diabetes mellitus is available.<sup>9,14–18</sup> However, there is scarce literature evaluating the stiffness of pancreas in routine outpatients in India.<sup>19</sup> Our SWE values were significantly higher than those in a pilot study conducted by Püttmann et al, who compared the SWE values between healthy patients and those with type 1 diabetes mellitus.<sup>20</sup> The values in normal patients were 1.0 (SD 0.2) m/s, and in the body of the pancreas was 1.2 (SD 0.2) m/s. The measurements were performed with a Siemens Acuson S3000 (Siemens Healthcare, Erlangen, Germany) using the Virtual Touch tissue quantification method. Possible explanations for the difference in the SWE values of our study and the study by Püttmann et al are the racial differences in pancreatic stiffness (the study was conducted on German subjects and patients) as well as the small sample sizes in the study by Püttmann et al.<sup>20</sup> In comparison, our data were collected from 205 subjects who were visiting the outpatient department for miscellaneous complaints. Although there are no studies reporting the racial differences in pancreatic stiffness, ethnic differences in pancreatic fat



**Fig. 3** Scatter plots showing the correlation of shear wave elastography of the pancreatic head (upper panel) and the body (lower panel) with age. As the age increases, the stiffness of the head as well as body of pancreas increases.

**Table 1** Shear wave elastography values in different age groups

Groups	Mean ( $\pm$ SD), kPa		Median, kPa		IQR, kPa		p-Value	
	Head	Body	Head	Body	Head	Body	Head	Body
$\leq 20$ y	7.98 $\pm$ 2.16	6.55 $\pm$ 2.01	8.31	6.55	6.12–10.2	4.43–7.95	0.034	0.003
21–40 y	8.68 $\pm$ 1.96	8.55 $\pm$ 2.14	8.81	8.22	7.26–9.27	7.12–10.1		
41–60 y	9.36 $\pm$ 2.11	9.17 $\pm$ 2.26	9.42	8.92	7.76–10.9	7.69–10.6		
> 60 y	9.43 $\pm$ 1.82	8.77 $\pm$ 2.57	8.81	8.07	8.22–11.6	7.48–11.1		

Abbreviations: IQR, interquartile range; kPa, kilopascal; SD, standard deviation.

accumulation as well as liver stiffness have been reported.<sup>21,22</sup> The mean age of the subjects in the study by Püttmann et al was lower (31.8 [SD 9.6] years). In another study, the SWE values of the pancreas in normal subjects were 1.44 (SD 0.39) m/s for women and 1.19 (SD 0.29) m/s for men. In the body, the results were 1.49 (SD 0.37) m/s for women and 1.26 (SD 0.30) m/s for men.<sup>1</sup> This study was also conducted using a Siemens Acuson S3000. The SWE values of the pancreas of our cohort are higher than another study reporting SWE of the pancreas in Indian patients. The mean values in the study by Nidhin et al in the head and body were 1.05 (SD 0.25) m/s and 1.17 (SD 1.1) m/s, respectively.<sup>19</sup> The differences in the pancreatic stiffness values in our study

compared with the published studies may be explained based on the different techniques/US equipment used in different studies. Most of the previously published studies have utilized pSWE-based ARFI, which is different from the technique (2D-SWE) used in the current study. Similar differences were reported in a study evaluating pancreatic stiffness by SWE in healthy children and adolescents.<sup>11</sup>

We found a regional variation in the SWE values in the head and body region. The elastography values were higher in the head than the body of the pancreas (although the difference was not statistically significant). The likely reason for this disparity was anatomical. The body is located deeper and more posteriorly than the head, which is relatively

**Table 2** Shear wave elastography values in different groups of patients

Groups	Mean SWE values ( $\pm$ SD), kPa		p-Value
	Head	Body	
Males	8.93 $\pm$ 2.5	8.75 $\pm$ 2.8	0.671
Females	9 $\pm$ 2.45	8.6 $\pm$ 2.6	0.798
No abnormality	8.6 $\pm$ 2.65	8.15 $\pm$ 2.5	0.451
CLD	9.05 $\pm$ 2.5	8.95 $\pm$ 3	0.981
Fatty liver	8.85 $\pm$ 2.25	9.4 $\pm$ 2.25	0.657
Gallstones	8.85 $\pm$ 2.45	8.35 $\pm$ 2.3	0.579

Abbreviations: CLD, chronic liver disease; kPa, kilopascal; SD, standard deviation; SWE, shear wave elastography.

superficial, which may attenuate the US waves leading to lower elastography values in the body. This finding is in agreement with that reported by Stumpf et al.<sup>1</sup>

Many studies report an increase in pancreatic elastography values with increasing age. Püttmann et al showed an increase in SWE and SWV values with increasing age.<sup>20</sup> This is in agreement with the finding in our study. The likely explanation for the increase in stiffness is the age-related fibrosis. Another reason could be the high incidence of diabetes mellitus among the elderly population. Diabetes is known to cause pancreatic inflammation and fibrosis.<sup>17</sup> However, Xie et al demonstrated that elastography in healthy adult volunteers did not significantly correlate with sex, age, height, weight, waist circumference, BMI, or organ dimensions.<sup>23</sup> We could not find any previous studies on the effect of fatty liver on the SWE of the pancreas. The studies by Nidhin et al and Xie et al showed that BMI had no impact on the SWE of the pancreas.<sup>19,23</sup> However, we found that SWE values were higher in patients with fatty liver. There is no published data on the effect of CLD and gallstones on pancreatic stiffness.

EUS has become the preferred modality for the evaluation of pancreas in many focal and diffuse pancreatic diseases.<sup>24</sup> This is due to the proximity of the EUS transducer to the pancreas. On the other hand, transabdominal US suffers from the interposition of various structures between the pancreas and the transducer. These include skin and subcutaneous tissue, and the stomach. However, several authors have successfully measured pancreatic stiffness using transabdominal US. Transabdominal SWE of pancreas is highly relevant as pancreatic elasticity on EUS is measured by strain ratio in the currently available systems. Strain elastography does not provide an absolute measurement of tissue elasticity and is inferior to SWE.<sup>25</sup> A recent study, however, evaluated the feasibility of EUS SWE in the evaluation of the pancreas.<sup>26</sup> EUS SWE was performed in focal pancreatic lesions, autoimmune pancreatitis, and normal pancreas. The authors reported EUS-SWE was feasible in most of the patients. However, in routine practice, the equipment and expertise for EUS may not be available at all centers. EUS-SWE also suffers from lack of objectivity. Although, MR elastography is an objective and promising method of assessment of pancreatic stiffness, it is currently performed routinely in very few centers.<sup>27</sup>

There were a few limitations to our study. The sample size was small, and we did not perform any formal sample

size estimation. We chose a convenience sample size. Although we included subject with no pancreas-related symptoms who had normal pancreas at transabdominal US, these parameters may not exclude early chronic pancreatitis. Additionally, there was an absence of a reliable gold standard of pancreatic stiffness. The accepted gold standard currently is histology. None of our patients underwent a pancreatic biopsy to confirm our elastography findings. However, pancreatic biopsy for this indication is neither feasible nor ethically appropriate. We included patients with CLD. Although we did not explicitly evaluate the cause and severity of CLD, it is possible that in many patients, alcohol abuse was the underlying cause. Chronic alcohol intake may also affect the pancreatic stiffness. The function of pancreas was not assessed. SWE values show a variation depending upon angle and depth of insonation. Beyond 8 cm depth, the values are unreliable due to the attenuation of waves by the subcutaneous fat. However, all our subjects were healthy with normal built and BMI. In patients with difficulty visualizing pancreas, maneuvers such as gastric distension with fluid and changing the patient to lateral decubitus position may help. Aortic pulsations also influence the values of SWE and SWV. However, it is impossible to remove this factor in humans. Other possible factors, such as transducer pressure and respiratory phase, also warrant further investigation.

In conclusion, our study gives the reference values of SWE for the normal pancreas. This nomogram may be used as a reference for further studies on elastography in various pancreatic pathologies in the Indian population. However, larger prospective studies are needed to provide definitive data on reference values of SWE.

#### Conflict of Interest

None declared.

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