

LETTER TO THE EDITOR

A Critique on the Article Describing "Pancreatic Mucinous Cystic Neoplasm Size Using CT Volumetry, Spherical and Ellipsoid Formulas: Validation Study"

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To the Editor,

We read with interest the article 'Pancreatic Mucinous Cystic Neoplasm Size Using CT Volumetry, Spherical and ellipsoid formulas: Validation Study' by Chalian *et al.* [1] published in the January 2014 edition of Journal of the Pancreas .JOP (online). We commend the authors for their valuable contributions towards establishing the accuracy and reproducibility of CT volumetry for pancreatic cysts. The article is excellent and informative. However, it would be of enormous help if the authors could clarify the queries we had while reading the manuscript.

Type of Study and Informed Consent

The authors mention the study to be a retrospective one where acquisition of CT was followed by the complete aspiration of 14 pancreatic mucinous cystic neoplasms (PMCNs) [1]. We would like to understand the indication for full aspiration of the cysts. Walsh *et al.* [2] reported minimal volume required to be aspirated for complete cyst analysis to be 2 ml [cytology (1ml), CEA (0.5 ml) and amylase (0.5 ml)]. Since in the present study 6 cysts as per observer 1 and 8 cysts as per observer 2 (table 1 of the original article) were more than 2 mL, the indication for full aspiration needs to be mentioned. In the absence of such an indication, complete cyst aspiration is a deliberate intervention for which informed consent of the patients explaining potential complications of full aspiration is warranted. We would like to understand the waiver of informed consent document in such a situation.

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Study Population: Pancreatic Mucinous Cystic Neoplasm

The manuscript includes comparison of CT volumetry, ellipsoid and spherical formula, with EUS guided aspirated volume for PMCNs. We would like to know as to how the pathologic characterization of the pancreatic cysts to be PMCN was done. Since the minimum volume of the cyst was 0.32 ml (refer table 1 of the original article), its characterization is not plausible by mere aspiration (as per Walsch minimal volume required is 2 ml [2]).

CT scan and Endoscopic Ultrasound (EUS) Guided Complete Aspiration

The manuscript in the introduction section states that EUS aspirated volume of the completely collapsed pancreatic cysts has been used to measure their actual volume [1]. The cited reference article [2], however, considers complete evacuation of small sized cysts only and not of all cysts.

Also the demographics section mentions the mean time interval between obtaining CT and performing EUS was 36±53 days [1]. We suggest that it should be clarified how time could be negative (in literal sense which could mean that EUS was performed before the computed tomography!) or if there is some hidden statistical concept. Besides, in a time span of 89 (36 + 53) days, the cyst size might change.

Inter-Observer Reproducibility

The text mentions the mean values for CT volumetry of 78 cysts to be 55.5 ± 155.9 ml and 53.5 ± 146.4 ml for observer #1 and observer #2, respectively [1]. These values include mean ± standard deviation. The standard deviation is usually not more than mean unless the data is highly skewed. In the present study the standard deviation 155.9 and 146.4 ml is higher than their respective mean values of 55.5 and 53.5 ml for the observers 1 and 2 respectively. In that case, mention of skewness is required.

Additionally, the reported r value for the 78 cysts is 0.997. According to Colton [3], correlations of 0.95 or greater should be viewed with caution in biologic sciences because of inherent variability in most biologic characteristics. Such a high r value in biologic sciences could be an error or an artifact [3].

EUS Aspiration for Volume Detection: The Gold Standard

There is a mention about EUS to be the gold standard for measuring the true volume of pancreatic cysts. Although the authors provide a reference for the same [2], the reference article does not speak of EUS as a gold standard [2]. Further, the successful EUS aspiration of the pancreatic cyst correlates with size and may not depend on its location [2]; mention of which is desirable.

Finally, there should be a mention of retrospective study in the title of the article. Besides, the comparator group i.e., Endoscopic ultrasound guided cyst aspiration should also be mentioned in the title (as per PICOT formula) [4].

The present study validates usage of CT volumetry for estimation of PMCN. Since the management for pancreatic cysts considers size of the cyst as a criterion and that pancreatic cysts are irregular in size, CT volumetry appears to be a promising tool. However, clarification of above mentioned aspects would make the study more robust.

Editorial Comment

The discussion and the debate are very appreciated in JOP since they contribute to a better knowledge in the scientific word. Thus we wish to receive and to publish the response from Dr. Chalian and Colleagues in order to complete this discussion by elucidating all the topics of the debate. In particular, Dr. Aswani and Colleagues in their very interesting comments, pay particular attention to some statistical details together with some other methodological and clinical questions.

The comment about the high intraclass correlation coefficient (ICC) between the two observers found from Dr. Chalian and colleagues for the CT volumetry is of a particular notice. As Aswani and Colleagues pointed out by suggesting the caution to be applied when such values occur in biologic sciences [3], higher values of correlation coefficients might be either indexes of an optimal relationship between two variables or indexes of the presence of possible artifacts. In this specific case, we deal about ICC instead of regression coefficients between variables, and, since there are no reasons for suspecting methodological errors in the Dr. Chalian and colleagues investigation, the most likely hypothesis to be taken into account is the probable good agreement between two observers instead of the presence of possible confounding factors that might be easily present in evaluating relationships between variables. Unfortunately, we cannot be able to conclusively solve this question in this discussion, but we hope that future works would investigate this topic by confirming the Dr. Chalian and colleagues results or, alternatively, by highlighting some reasons for the presence of artifacts.

Another statistical topic discussed from Dr. Aswani and colleagues is the presence of a value of standard deviation greater than the mean value as far as the time interval between obtaining CT and performing EUS is concerned. This absolutely does not mean that negative values

are present or that, alternatively, there is some hidden statistical concept, as Dr. Aswani and colleagues stated. This finding only suggests that a skewed distribution of the data is present and it does not involve any statistical problem. It is well known that time intervals (like duration of follow-up, etc.) commonly present skewed distributions with often standard deviation values greater than the mean ones; in particular, these data may have a Poisson distribution (which is characterized by a standard deviation value equal to the mean value) that is a fundamental distribution in the queuing theory. We would like to suggest to Dr. Chalian and colleagues of reporting some more statistics in order to describe these skewed data (like, ranges, interquartile (IQR) and/or other percentile values, etc.), thus integrating the limited information carried-out by reporting mean and DS values only.

Finally, this last suggestion can be also applied to the comment made from Dr. Aswani and colleagues about the skewed distribution of the CT volumetry. At this regard some concerns might be risen since Dr. Chalian and colleagues have applied parametric tests. It should be pointed out that these authors correctly applied within subject analyses (i.e., paired t-test and repeated measure ANOVA) that require a normal distribution of the within-subject data (i.e., the distribution of the differences between pairs). Thus, the skewed distributions of the overall data highlighted by Dr. Aswani and colleagues cannot be considered at a glance a fault in the analysis since these distributions take into account both the between- and the within-subject variabilities, but, in this case, the normal distribution of the differences between pairs need to be tested. This last comment pleads for the use of non-parametric tests because these tests allow robust, reliable and easy analyses in these occasions.

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Conflict of Interest

Authors declare to have no conflict of interest.

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