Functional tumour volume and peritoneal carcinomatosis to identify suitable candidates for cytoreductive surgery in ovarian carcinoma: abridged secondary publication

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KEY MESSAGES

1. Peritoneal carcinomatosis (PC) is a negative predictor of achieving complete cytoreduction in ovarian carcinoma.
2. Functional peritoneal cancer index (fPCI) is a novel non-invasive score based on the functional tumour volume derived from diffusion-weighted imaging (DWI) and the number of critical sites affected by PC.
3. fPCI is highly correlated with surgical PCI derived from laparotomy.
4. fPCI could predict the likelihood of complete cytoreduction with high accuracy in ovarian carcinoma.

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Introduction

The primary treatment for ovarian carcinoma is complete cytoreductive surgery (CRS). However, an upfront CRS is not always achievable due to the burden of peritoneal carcinomatosis (PC) and the disease extent. Neo-adjuvant chemotherapy followed by interval debulking surgery could be an alternative. PC is a negative predictor of achieving complete CRS. The best method to assess surgical resectability is by evaluating PC in the intraperitoneal cavity through laparotomy or laparoscopy. Peritoneal cancer index derived at surgery (sPCI) is a validated score, which measures the extent of PC. A high sPCI and involvement of critical sites by PC in and around the mesenteric vessels, bowel serosa, and porta hepatis reduce the likelihood of successful CRS.

Computed tomography is the most utilised non-invasive imaging modality in pre-operative evaluation of ovarian carcinoma and PC. A predictive model that incorporated information of PC size and distribution has been proposed to determine surgical resectability and predict the likelihood of achieving complete CRS. However, this predictive model is dependent on the radiologist's experience and a degree of subjectivity in the assessment, and hence it has not been generalisable to other cohorts.[1]

Diffusion weighted imaging (DWI) is a functional sequence on magnetic resonance imaging (MRI). It is superior to computed tomography in tumour characterisation, staging and depiction of PC. The derived apparent diffusion coefficient (ADC) reflects tumour cellularity and disease aggressiveness. Therefore, DWI has the potential in quantifying PC burden and in predicting the likelihood of surgical success.

The aims of our study were (1) to construct a new method in assessing PC tumour burden by incorporating functional tumour volume (FTV) derived from DWI and the PC spread pattern to form the functional peritoneal cancer index (fPCI); (2) to design a predictive model consisting of fPCI and clinical factors for predicting the likelihood of achieving complete CRS / interval debulking surgery; and (3) to investigate the relationship between tumour biology of PC and surgical resectability.

Methods

Patients with advanced (FIGO III/IV) or recurrent ovarian carcinoma were assessed with DWI before CRS / interval debulking surgery. Clinicopathological information including age, FIGO staging, and pre-surgical (time interval, <14 days) serum cancer antigen 125 (CA-125) level were documented.

Standard T2-weighted imaging was performed using a 3.0 T MRI platform for the abdominopelvic area in two planes with additional sagittal plane covering the pelvis. DWI was acquired with 3 *b* values (0, 400, 800 s/mm^2) in free breathing in the axial plane, with the same anatomical coverage as the conventional sequences. The ADC maps were constructed using Matlab R2019a (The MathWorks,

Natick, Massachusetts, USA).

During surgery, patients were assessed for PC burden using sPCI. The abdominopelvic cavity was arbitrarily divided into 13 regions (right upper quadrant, epigastrium, left upper quadrant, right flank, umbilical region, left flank, right lower quadrant, pelvis, left lower quadrant, mesentery and serosa in upper jejunum, lower jejunum, and upper ileum and lower ileum). A sPCI score of 0 was given when there was no PC. When PC was present, the largest one lesion was selected as the target lesion and was scored as 1 when <0.5 cm, 2 when 0.5-5.0 cm, and 3 when >5.0 cm. The immediate surgical outcome was dichotomised into complete and incomplete cytoreduction. The surgical duration and the number of surgical subspecialties involved were documented.

Volumes of interest for the calculation of FTV (VOIs-FTV) was drawn on all slices that the tumour existed in for all PC lesions on b=800 s/mm^2 and transferred to ADC maps. Using K-means clustering, the intermediate ADC cluster of each patient was regarded as the solid tumour component with high cellularity and was used for FTV calculation. The high ADC cluster was considered as normal or cystic tissues and low ADC cluster was regarded as fibrous or fat tissues, which were subsequently discarded.[2] A score of 0 to 3 was assigned to each region as in sPCI and additional points were given to each critical site involved by PC at the mesentery, serosa or porta hepatis to form the fPCI.

The largest PC lesion of each patient was chosen as the target lesion for the measurement of ADC. Volumes of interest for the measurement of ADC (VOIs-ADC) were drawn very strictly along the margin on all slices that the tumour existed on b = 800 s/mm^2 images and transferred to ADC maps. The average of ADC within VOIs-ADC was calculated.

The correlations were assessed by Pearson coefficient correlation (r). Univariate and multivariate logistic regressions were used to generate prediction model that included fPCI, sPCI or ADC as predictors combined with age, FIGO staging and pre-surgical CA125 level. The receiver operating characteristic (ROC) curves were generated. A P value of <0.05 was considered statistically significant.

Results

A total of 51 patients aged 20 to 82 (mean, 56) years with advanced or recurrent ovarian carcinoma were included in the analysis. Complete cytoreduction was achieved in 33 (64.7%) patients, and the remaining 18 (35.3%) patients had incomplete cytoreduction.

Significant correlations were found between fPCI and sPCI on patient-based analysis (r=0.774, P<0.001) and region-based analysis (r=0.777, P<0.001). The mean fPCI and sPCI were significantly higher in the patients with incomplete cytoreduction than patients with complete cytoreduction (10.00 vs 4.36 and 12.06 vs 5.70, respectively, both P<0.05); whereas the opposite was found in ADC (1.30 vs 1.52, P=0.040, Fig 1). Both fPCI and sPCI were moderately correlated with surgical duration (r=0.524, P<0.001 and r=0.632, P<0.001, respectively), but only modestly with the number of surgical subspecialties involved (r=0. 402, P=0.003 and r=0.396, P=0.004, respectively).

fPCI, sPCI and ADC were significant in univariate analysis (P<0.05). Age, staging, and pre-surgical CA125 levels were identified as independent prognostic variables. Multivariable models of fPCI, sPCI, and ADC, each including the previously identified 3 clinicopathological factors, could achieve accuracy of 92.2%, 80.4%, and 74.5%, respectively (area under ROC curves were 0.956, 0.909, and 0.788, respectively). There was no significant difference between fPCI and sPCI in predicting surgical outcome (P=0.202), but both outperformed ADC (fPCI vs ADC, P=0.007; sPCI vs ADC, P=0.034, Fig 2).

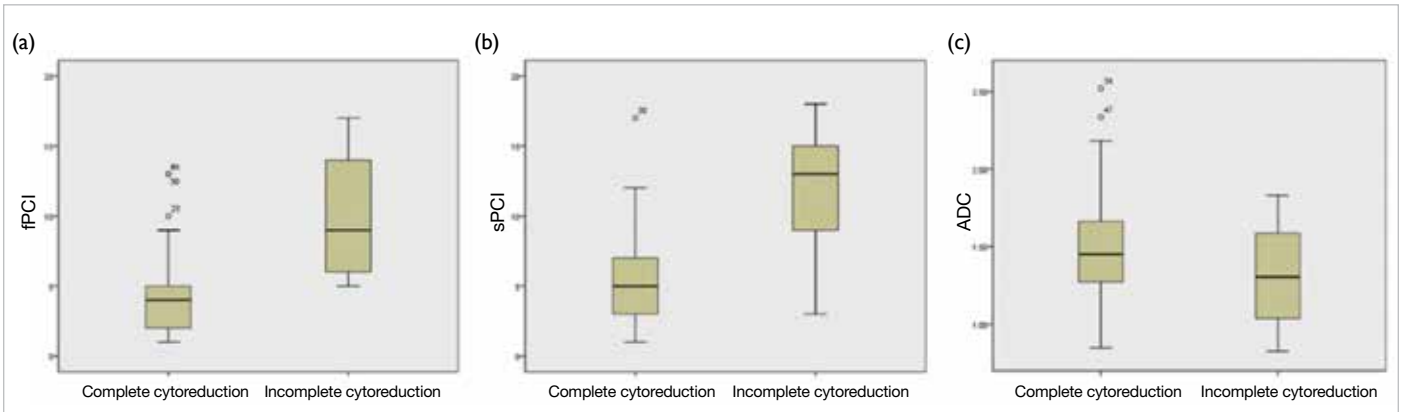

FIG 1. Comparison of (a) functional peritoneal cancer index (fPCI), (b) surgical peritoneal cancer index (sPCI), and (c) apparent diffusion coefficient (ADC) in patients with complete and incomplete cytoreduction.

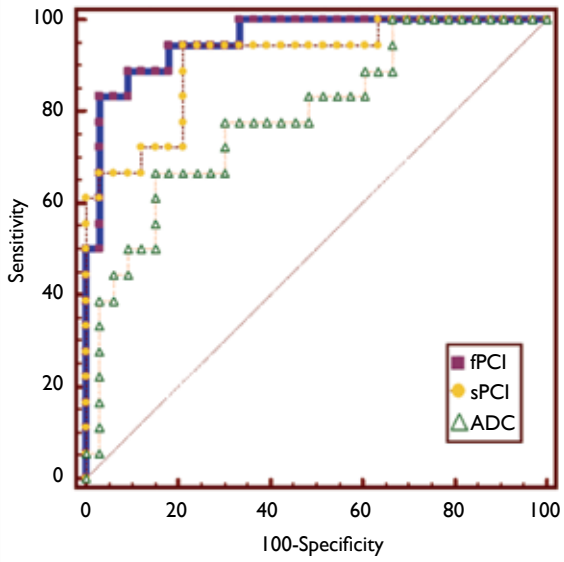

FIG 2. Receiver operating characteristic curves for functional peritoneal cancer index (fPCI), surgical peritoneal cancer index (sPCI), and apparent diffusion coefficient (ADC) in predicting tumour resectability.

Discussion

Our novel method of delineating PC using DWI is done by assessing PC tumour burden and disease spread and quantifying this information into an fPCI. A scoring system based on fPCI can predict the likelihood of complete cytoreduction in advanced and recurrent ovarian carcinoma.

K-means clustering has been shown to be able to differentiate malignant and benign tissues: the presence of benign fibrous tissues containing dense networks of collagen fibres and abundant collagen-producing fibroblastic cells would decrease the ADC value, whilst oedema, haemorrhage and cysts with hypocellular areas of loose oedematous connective tissue would result in a higher ADC value.[2] Hence, the intermediate ADC cluster that represented tumour with high cellularity was subsequently used to calculate the FTV.

fPCI has similar predictive value to sPCI in determining the likelihood of achieving complete cytoreduction.[3] fPCI has high agreement with sPCI.[4] In addition, we evaluated a semi-automated method in depicting tumour volume based on tumour cellularity. Considerations were given to critical sites and other clinicopathological factors that could impact surgical success.

Conclusion

fPCI, a non-invasive scoring system, can provide a quantitative means of evaluating tumour burden and disease spread. It has high correlation with sPCI in advanced or recurrent ovarian cancer. fPCI and ADC derived from DWI achieve a moderate-to-high accuracy in predicting success of cytoreduction, potentially aiding in patient's selection for cytoreduction and treatment stratification.

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Disclosure

The results of this research have been previously published in:

1. An H, Lee EYP, Chiu K, Chang C. The emerging roles of functional imaging in ovarian cancer with peritoneal carcinomatosis. Clin Radiol 2018;73:597-609.
2. Lee EYP, An H, Perucho JAU, et al. Functional tumour burden of peritoneal carcinomatosis derived from DWI could predict incomplete tumour debulking in advanced ovarian carcinoma. Eur Radiol 2020;30:5551-9.

References

1. Axtell AE, Lee MH, Bristow RE, et al. Multi-institutional reciprocal validation study of computed tomography predictors of suboptimal primary cytoreduction in patients with advanced ovarian cancer. J Clin Oncol 2007;25:384-9.
2. Gong NJ, Wong CS, Chu YC, Guo H, Huang B, Chan Q. Increasing the accuracy of volume and ADC delineation for heterogeneous tumor on diffusion-weighted MRI: correlation with PET/CT. Int J Radiat Oncol Biol Phys 2013;87:407-13.
3. Engbersen MP, Van T Sant I, Lok C, et al. MRI with diffusion-weighted imaging to predict feasibility of complete cytoreduction with the peritoneal cancer index (PCI) in advanced stage ovarian cancer patients. Eur J Radiol 2019;114:146-51.
4. Gadelhak B, Tawfik AM, Saleh GA, et al. Extended abdominopelvic MRI versus CT at the time of adnexal mass characterization for assessing radiologic peritoneal cancer index (PCI) prior to cytoreductive surgery. Abdom Radiol (NY) 2019;44:2254-61.