A Cohort Study to Decode the Application of Peritoneal Carcinomatosis Index in Predicting the Prognosis of Advanced Ovarian Malignancies

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ABSTRACT

Introduction: Peritoneal Carcinomatosis Index (PCI) is used to assess the extent of peritoneal cancer by dividing the peritoneal cavity into 13 well-defined regions and assessing the size of the largest tumour nodule in each region.

Aim: To evaluate the imaging features of peritoneal carcinomatosis using Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) and correlate it with diagnostic laparotomy. Also to determine the prognostic significance of peritoneal carcinomatosis index calculated radiologically, in predicting the outcome of advanced ovarian malignancies.

Materials and Methods: This was a prospective cohort study conducted in Kilpauk Medical College, Chennai, Tamil Nadu, India, from July 2019 to December 2020. Total of 50 females between 18-80 years of age with advanced ovarian malignancies with peritoneal deposits underwent CT and MRI to calculate initial PCI. Then these patients underwent cytoreductive debulking after which final response was assessed. Followed-up for a period of 1 year to assess the treatment response and to look for any complications. IBM Statistical Package for the Social Sciences (SPSS) version 22.0 software was used for statistical analysis. Descriptive analysis was carried out using mean and standard deviation for quantitative variables.

Results: Fifty females were included with a mean age of 53.4 years. PCI calculated using CT and MRI showed strong correlation with laparoscopic PCI with correlation coefficient (r) of 0.984 and 0.988 respectively with a statistically significant p-value <0.001. Initial radiological PCI and cytoreduction showed strong correlation when analysed using ROC curve (Receiver Operating Characteristic curve) with an AUC (Area under the ROC Curve) of 0.933. With Youden index, a cut-off value of 11 was derived under which patients had optimal cytoreduction and a better outcome. Radiological PCI showed good sensitivity (82.35%) and specificity (88.78) for predicting complications and it was found that patients with PCI >15 were at a higher risk for developing various complications.

Conclusion: Radiological PCI strongly correlate with laparoscopic PCI and is a very strong predictor of disease outcome in advanced ovarian malignancies. It was found that patients with high PCI values had poor response to cytoreductive surgery and chemotherapy. So, high initial PCI values above 11 was indicative of poor patient prognosis.

Keywords: Chemotherapy, Cytoreduction, Laparoscopy, Metastasis

INTRODUCTION

Ovarian cancer is one of the leading gynaecologic cancers that has the highest mortality rate among females in various parts of the globe. Many of the cases are being detected in late stages and these patients are having poor clinical outcome. Ovarian cancers are known to show peritoneal deposits [1]. In ovarian malignances, peritoneal seeding is the most common pathway for the tumour cells to slough off from the ovary and enter the peritoneal circulation and seed into multiple sites and get deposited there [2]. The detection of these peritoneal deposits is important in the staging and follow-up of ovarian cancer. To find out the extent of intraperitoneal tumour dissemination and its impact in surgical cytoreduction and survival, many studies has been conducted in colorectal/gastric cancers and a numerical score termed Peritoneal Cancer Index (PCI), was developed [3].

Peritoneal Cancer Index is an index that can assess the extent of peritoneal cancer throughout the peritoneal cavity by dividing the peritoneal cavity into 13 well-defined regions and assessing the size of the largest tumour nodule in each region [4]. So, it is essential to have an idea about the relationship between peritoneal spread of the disease and patient outcome whether the amount of peritoneal disease have any impact in treatment response and patient survival [5]. The present study aimed to assess how radiological PCI correlates with surgical PCI. It also attempted to study the impact of PCI in predicting the outcome of advanced ovarian malignancies, by finding out a cut-off value above which the patients are having sub-optimal cytoreduction and poor outcome.

MATERIALS AND METHODS

This is a prospective cohort study, conducted in the Department of Radiodiagnosis in Government Kilpauk Medical College, Kilpauk, Chennai, India, from July 2019-December 2020. Females between 18-80 years of age with advanced ovarian malignancies and peritoneal deposits and those who did not received any previous treatment for malignancy were considered as the study population. A sample size of 50 was considered for the present study (when the proportion with good prognosis is taken as 60%, a sample size of 50, would achieve results with 95% confidence interval, with an accuracy of 10%). Ethical committee approval was obtained (Protocol ID 233/2019).

Inclusion criteria: Patients with advanced ovarian carcinoma having peritoneal deposits and those patients undergoing both CT and MRI as a part of metastatic work-up were included in the study.

Exclusion criteria: Carcinoma ovary patients without peritoneal deposits, other carcinomas with peritoneal deposits, patients not undergoing both CT and MRI, contraindication to contrast administration and those who are reluctant to participate in the study were excluded from the study.

Procedure

After giving detailed explanation about the study and obtaining informed consent, both contrast CT and MRI were taken. CT was performed on 16-slice MDCT (Toshiba aquilion). MRI is performed using 1.5 Tesla MRI (SIEMENS) and sequences used were T1, T2 axial, T2 coronal and from them Diffusion Weighted Imaging (DWI) sequences were obtained. The CT protocol included unenhanced, arterial, and portal phase evaluation of abdomen. Then with CT and MRI, radiological PCI score was calculated [6]. And the laparoscopic PCI was assessed after undergoing diagnostic laparotomy. Correlation between initial radiological PCI and laparoscopic PCI was calculated. After calculating initial PCI value radiologically and comparing it with laparoscopic PCI values, the patients were categorised into four groups based on initial PCI values:

- Group 1 as PCI value 1-7
- Group 2 as PCI value 8-13
- Group 3 as PCI value 14-25
- Group 4 as PCI value 26-39

After completing the neoadjuvant chemotherapy, CT and MRI was repeated for assessing the response and to calculate decrease in disease load. Further the patients underwent cytoreductive debulking surgery. Then the cytoreduction was categorised as optimal or suboptimal according to presence of macroscopic residual disease. Correlation between initial radiological PCI and treatment response in the form of cytoreduction was also studied. The patients were then followed-up for a period of one year after cytoreductive debulking surgery to assess the treatment response and to look for any complications.

The method of calculating PCI is shown in [Table/Fig-1]. PCI index was calculated by dividing the peritoneal cavity into 13 well-defined regions and assessing the size of the largest tumour nodule in each region. Deposit <0.5 cm will be given 1 point. Deposit up to 5 cm will be given 2 point and deposit >5 cm will be given 3 points.
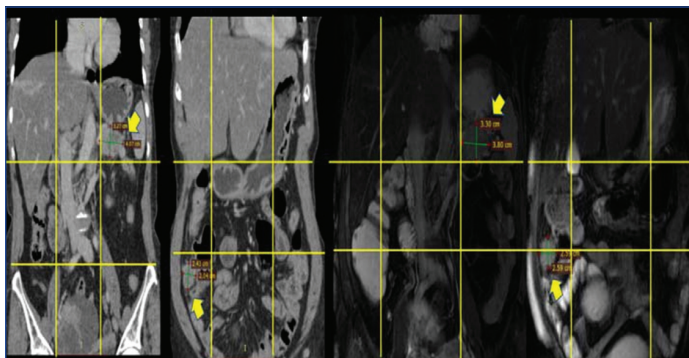
[Table/Fig-1]: Calculating Peritoneal Carcinomatosis Index (PCI) (3) (6) CECT and MRI images showing deposits in left hypochondrium, right iliac fossa.
[Yellow arrows- denotes the peritoneal deposits]; [Numbers- corresponds to the size of deposit]

STATISTICAL ANALYSIS

The data was entered in a excel worksheet and were double checked. IBM SPSS version 22.0 software was used for statistical analysis. Descriptive analysis was carried out using mean and standard deviation for quantitative variables. The frequency and proportion were used for categorical variables. Regression analysis correlation test was done to determine the strength of association between the comparing variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots. The p-value <0.05 was considered as statistically significant.

RESULTS

Fifty females were included in the present study with age group ranging between 18-75 years with a mean age of 53.4 years. For

these patients with advanced carcinoma ovary with peritoneal metastasis, radiological PCI score was calculated with help of CT and MRI and was compared with laparoscopic PCI [Table/Fig-2-5].
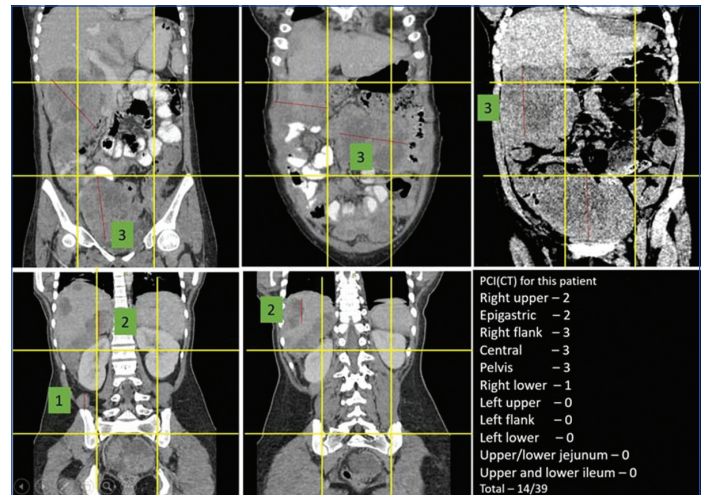

[Table/Fig-2]: Largest deposit from each 13 quadrant is measured and sum is obtained. Total score is given out of 39.
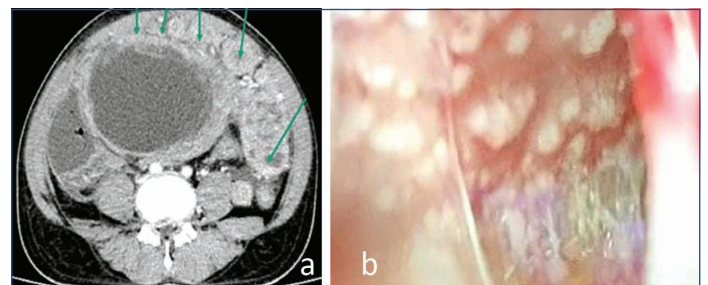
[Table/Fig-3]: a) CECT abdomen shows multiple peritoneal deposits (PCI CT=16); b) Intraoperative image shows multiple peritoneal deposits (PCI lap=18).
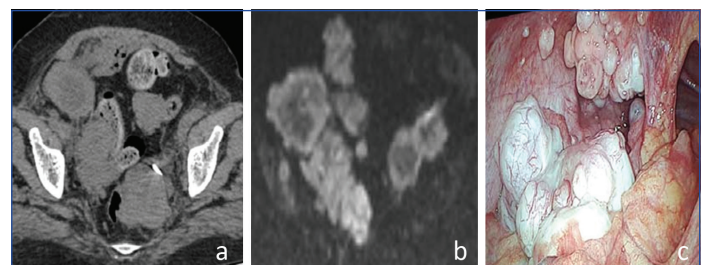
[Table/Fig-4]: a) CT image showing deposits in pelvis; (CTPCI-18) b) MR image showing deposits in pelvis (MRI PCI 19) ; c) Intraoperative confirmation of deposits in pelvis (Lap PCI 19).
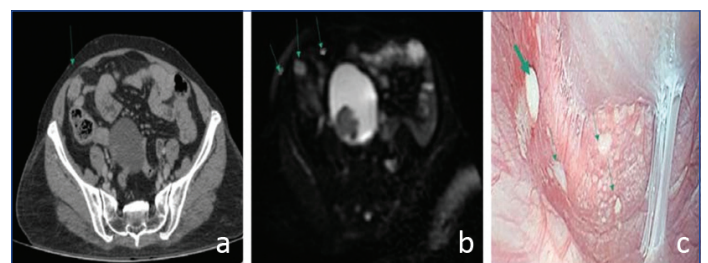
[Table/Fig-5]: a) Single deposit seen in CT; b) Few more tiny deposits seen in DWI; c) Multiple tiny deposits seen in laparoscopy.

Case-1 [Table/Fig-2]: A 56-year-old female with carcinoma ovary and multiple peritoneal deposits.

Case-2 [Table/Fig-3]: A 55-year-old female with multiple large ovarian mass and peritoneal deposits. CECT showed good sensitivity in picking up peritoneal deposits and was comparable to the PCI index obtained from laparoscopy.

Case-3 [Table/Fig-4]: A 64-year-old female with histologically proven serous cystadenocarcinoma with multiple peritoneal metastasis. The patient had CT PCI value of 18 and MRI PCI of 19.

The deposits detected in CT and MRI were confirmed by laparoscopic evaluation. CT and MRI had good ability to detect the deposits larger than 10 mm.

Case-4 [Table/Fig-5]: A 49-year-old female, known case of mucinous cystadenocarcinoma ovary-postchemo-postcytoreduction status. Follow-up CT showed a single deposit in right iliac region, DWI images showed few more deposits in the adjacent region which was confirmed by laparoscopy. DWI MRI picks up more tiny deposits than CECT, but lesion less than 5 mm was missed even in DWI MRI.

Initial PCI calculated using CT and MRI scan were compared with laparoscopic PCI and plotted in a regression analysis curve. Both PCI calculated using CT and MRI showed strong correlation with laparoscopic PCI with correlation coefficient (r) of 0.984 and 0.988, respectively with a statistically significant p-value <0.001 [Table/Fig-6].
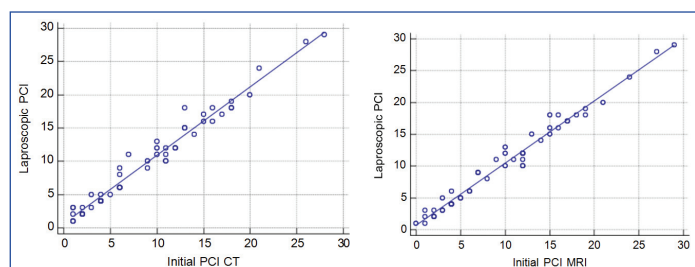
[Table/Fig-6]: Scatter plots showing correlation between initial PCI (CT and MRI) and laparoscopic PCI. Both PCI calculated using CT and MRI showed strong correlation with laparoscopic PCI.

The slight stronger correlation of PCI (MRI) over PCI (CT) was found to be because of its better soft tissue resolution. After calculating initial PCI value radiologically and comparing it with laparoscopic PCI values, the patients were categorised into four groups based on initial PCI values as mentioned above. Then the patients were subjected for neoadjuvant chemotherapy to down stage the disease. One month after the completion of neoadjuvant chemotherapy, repeat CT and MRI was taken for this patient to look for response assessment and again postchemo PCI values were calculated [Table/Fig-7,8].

Postchemo PCI CT	Initial PCI CT			
	Group 1	Group 2	Group 3	Group 4
0	19	3	0	0
Group 1	3	9	3	0
Group 2	0	4	5	1
Group 3	0	0	1	1
Group 4	0	0	1	0
Total	22 (44.0%)	16 (32.0%)	10 (20.0%)	2 (4.0%)

[Table/Fig-7]: Inter-rater agreement (kappa) between initial PCI CT and postchemo PCI CT.
Weighted kappa- 0.245, Standard error-0.052 and 95% CI 0.143 to 0.347

Postchemo PCI MRI	Initial PCI MRI			
	Group 1	Group 2	Group 3	Group 4
0	19	1	0	0
Group 1	2	11	4	0
Group 2	0	2	6	1
Group 3	0	0	2	1
Group 4	0	0	1	0
Total	21 (42.0%)	14 (28.0%)	13 (26.0%)	2 (4.0%)

[Table/Fig-8]: Inter-rater agreement (kappa) between initial PCI MRI and post chemo PCI MRI.
Weighted kappa-0.247, Standard error-0.051 and 95% CI-0.147 to 0.348

In group 1, 19 patients had complete response to chemotherapy and had no deposits (PCI=0). Three patients had postchemo PCI value with in 7 so that they were again classified under group 1.

In group 2, three patients got complete response to chemotherapy and had no deposits (PCI=0). Nine patients had good response and were downgraded to the 1st group. Four patients were not showing much response and remained same under group 2.

In group 3 and 4, no patients had complete response. Five patients from group 3 were downgraded to group 2. Group 3 and 4 patients showed only minimal reduction in postchemo PCI value.

Better response to chemotherapy was obtained for group 1 (PCI 1-7) and as the PCI value increased, the response to chemotherapy decreased. After neoadjuvant chemotherapy, these patients were subjected for cytoreductive surgery. The outcome of the surgery was classified into optimum and suboptimum according to the clearance obtained during the surgery. If surgeons were able to remove all the deposits from peritoneum along with uterus and ovaries, they labelled it as optimal cytoreduction and if they were not able to get complete clearance, those cases were labelled as sub-optimal cytoreduction.

The four different histological patterns of ovarian carcinoma in the present study were: (1) Germ cell tumours; (2) Mucinous cystadenocarcinoma; (3) Endometrioid Ovarian tumours; (4) Serous cystadenocarcinoma. Response to platinum-based chemotherapy in each of these histological groups was assessed by calculating the percentage decrease in PCI index using the formula. Among the four histological sub-types, two cases of endometrioid ovarian tumours showed good response to chemotherapy with a mean percent decrease of 88.88%.

The majority of cases belonged to serous cystadenocarcinoma (28/50). These histological variants also showed very good response to platinum-based chemotherapy with a mean percent decrease of 79.82%. Mucinous cystadenocarcinoma comprised of (15/50) cases, these group did not show response to platinum-based chemotherapeutic agents as compared to other three groups. Mean percent decrease showed by this group was only 57.60% [Table/Fig-9].
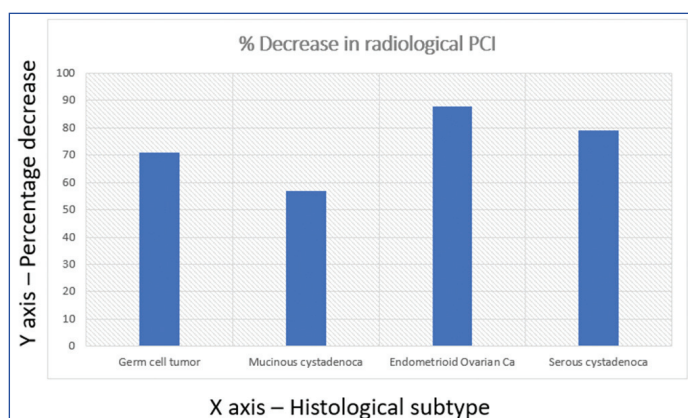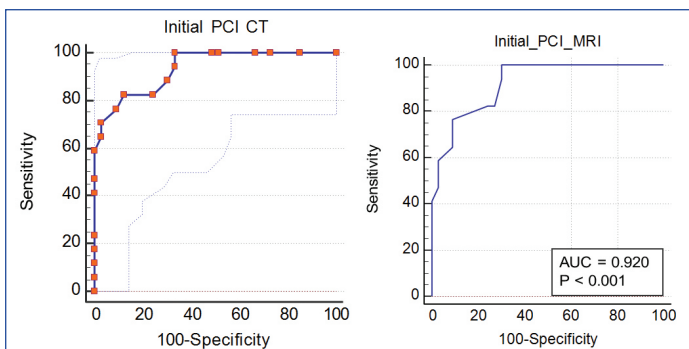

[Table/Fig-9]: Percentage decrease in PCI CT postchemo among various sub-types.

Initial radiological PCI value and cytoreduction shows strong correlation, as the initial PCI value increases, there is more chance for that patient to have sub-optimal cytoreduction [Table/Fig-10].

With Youden index, it was found that the cut-off value of 11 with a sensitivity of 82.35 and specificity of 87.88. When CT PCI value goes above 11, there are more chances for sub-optimal cytoreduction for those patients and they will be having a poor outcome. And when the CT PCI value is less than 11, those patients were found to have optimal cytoreduction and having a better outcome [Table/Fig-11].

For predicting the patients who are at high risk for developing various complications of disease process, radiological PCI values were

[Table/Fig-10]: ROC curve plotted for cytoreduction vs initial PCI. CT and MRI shows initial radiological PCI value and cytoreduction shows strong correlation, as the initial PCI value increases there is more chance for that patient to have a sub-optimal cytoreduction.

Variables	Values
Area under the ROC curve (AUC)	0.933
Standard Error	0.0342
95% Confidence interval	0.825 to 0.984
z statistic	12.653
Significance level P (Area=0.5)	<0.0001
Youden index (J)	0.7023
Associated criterion	>11
Sensitivity	82.35
Specificity	87.88

[Table/Fig-11]: Results from ROC for cytoreduction vs initial PCI CT.

calculated using CT and MRI which were having very high sensitivity and specificity. With help of Youden index, a cut-off value of 15 was obtained. That means, whenever the radiological PCI value is more than 15, those patients are at a higher risk for developing various complications, related to the disease process [Table/Fig-12].
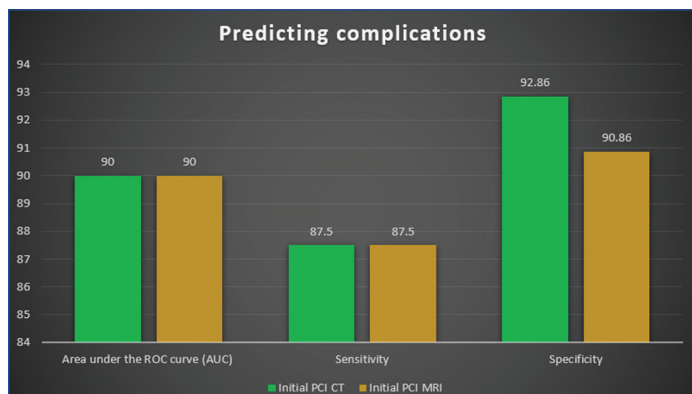
[Table/Fig-12]: Bar diagram showing role of PCI CT and PCI MRI in predicting complications.

DISCUSSION

Initial radiological PCI calculated using CT and MRI was compared with laparoscopic PCI and plotted in a regression analysis curve. It showed very strong relation between the two variables with correlation coefficient (r) of 0.984 and 0.988, respectively with a statistically significant p-value <0.001. Similar study done by Chan JK et al., showed similar results for correlation between radiological PCI (CT) and intraoperative finding was very high with a correlation coefficient of around 0.882 [7]. PCI scores calculated with CT and MRI, showed strong correlation with each other with a correlation coefficient (r) of 0.99 and with statistically significant p-value <0.001 and a strong kappa agreement of 0.91964.

This was in agreement with Kim A et al., study which showed CT and MRI were equal when read by experienced Radiologist [8]. CT shows better results when read by an experienced Radiologist compared to MRI, however the results of the latter can easily be

improved. In the present study, better response to chemotherapy was obtained for group 1 (PCI 1-7) and as the PCI value increased, the response to chemotherapy decreased. In the study of Halkia E et al., patients with a peritoneal cancer index lower than 10 had a significantly better survival than those with a PCI greater than 10 [9]. This slight difference may be due to the difference in ethnicity of people.

In a study conducted by Elzarkaa AA et al., patients with PCI score >13, were more prone for sub-optimal surgical cytoreduction, this was in agreement with current study [10]. Major share of the lesions belonged to serous cystadenocarcinoma (28/50) and this sub-type had a good response to chemotherapy showing significant reduction in postchemo PCI. Mucinous cystadenocarcinoma comprised of (15/50) cases, which did not show response to platinum-based chemotherapeutic agents as compared to other three groups. This was in agreement with study of Berkenblit A and Cannistra SA in which they found out that mucinous ovarian carcinoma has a poorer prognosis compared with other histological sub-types [11]. This was not in agreement with Bolis G et al., which showed that mucinous or endometrioid tumours have more favorable prognosis than serous tumours [12]. This change in response may be due to the difference in ethnicity and racial differences.

Limitation(s)

The present study was conducted in a single centre with a small sample size of 50 people for 18 months. It would be better to conduct this, as a large scale multicentric study with more sample size and follow-up for five years, to obtain more details regarding the relation between PCI and outcome.

CONCLUSION(S)

Radiological PCI calculated using CT and MRI showed strong correlation with laparoscopic PCI. Better response to chemotherapy was obtained for group 1 (PCI 1-7) and as the PCI value increases, the response to chemotherapy goes on decreasing. Among the four histological sub-types, endometrioid ovarian tumours and serous cystadenocarcinoma showed good response to chemotherapy and mucinous cystadenocarcinoma had poor response. Initial radiological PCI value and cytoreduction show strong correlation, as the initial PCI value increases, there is more chance for that patient to have a sub-optimal cytoreduction. A cut-off value of 11 was derived for radiological PCI, above which surgical outcome was sub-optimal with a poor prognosis. So, radiological PCI is an excellent indicator to predict the disease outcome in advanced ovarian malignancies.

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