ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 68 . 16
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 5, Issue – 5, October - 2020, Page No. : 73 - 80

A histopathologic chemotherapy response score assessment for ovarian /adnexal high-grade serous carcinoma

[1]Dr. Sirisha Kanukuntla, Assistant professor**,** Department of pathology, Kamineni academy of medical sciences and research center, LB nagar, Hyderabad.

[2]Dr. Saleem, Assistant Professor**,** Kamineni academy of medical sciences and research center, LB nagar, Hydearbad, Telangana.

[3]Dr. Ashok Kumar Deshpande, Professor &HOD, Kamineni academy of medical sciences and research center, LB nagar, Hyderabad.

[4]Dr. N.Vivekananda , Professor , Kamineni academy of medical sciences and research center, LB nagar, Hyderabad.

[5]Dr. K. Roopa, 3rd year PG , Kamineni academy of medical sciences and research center, LB nagar, Hydearbad,Telangana

Corresponding Author: Dr. Saleem, Assistant Professor**,** Kamineni academy of medical sciences and research center, LB nagar, Hydearbad, Telangana.

Citation this Article: Dr. Sirisha Kanukuntla, Dr. Saleem, Dr. Ashok Kumar Deshpande, Dr. N.Vivekananda, Dr. K. Roopa, "A histopathologic chemotherapy response score assessment for ovarian /adnexal high-grade serous carcinoma.", IJMSIR- October - 2020, Vol – 5, Issue - 5, P. No. 73 – 80.

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Introduction

Ovarian neoplasms most common neoplasms among the females and can arise from the ovarian epithelium, germ cells or the sex cord stroma. Approximately 1.3% of women are diagnosed with ovarian cancer at some point during their lifetime[1]. About 11.4 per 100000 women per year of new cases and about 7.0 per 100000 women per year deaths occur as a result of this disease, based on 2012-16 data[2]. It remains fifth most common cause of cancer death in women and leading cause of death from gynaecologic cancer[1,2]. Risk factors include strong family history, nulliparity, early menarche, late menopause, increasing age and white race. Oral contraception usage and pregnancy are associated with a decreased risk. Clinically they present with vague nonspecific symptoms of abdominal bloating, distension, dyspepsia, early satiety, anorexia, weight loss or constipation. They are often treated for gastrointestinal problems such as gastritis, irritable bowel syndrome, gall bladder disease. General examination may include ascites, pleural effusion or an abdominal mass. Neoadjuvant chemotherapy (NACT) followed by interval debulking has become a viable treatment option for advanced stage extrauterine high grade serous carcinoma (HGSC). For those treated with NACT a 3-tier chemotherapy response score based on histopathologic features had been proposed. Aim of the present study is to evaluate the chemotherapy response score in the omentum and adnexa to determine if the CRS correlates with the progression free survival or overall survival.

Materials and methods

A retrospective study of all surgically resected specimen of ovarian neoplasms from June 2015 to June

2020 were studied. A total of 27 cases were identified. With 24 cases were determined to have neo adjuvant chemotherapy. Available clinical data including patient history, clinical presentation, investigations, intra-operative surgical findings were reviewed. Resected specimens with high grade serous carcinoma histotype, in which the adnexa and omentum were removed in the same surgical procedure were included in the study. The weight and gross measurements were recorded. The capsule is inspected for areas of rupture, adhesions, tumour involvement or other abnormalities. Solid, cystic and papillary lesions are thoroughly sampled. Colour, consistency of the cystic fluid was noted. After adequate fixation representative sections were submitted for histopathological examination and characterisation of tumour was done according to recent WHO classification of ovarian tumours. Chemotherapy response score (CRS) was assessed in cases which received prior NACT. Chemotherapy response score was originally described by Bohm et al was summarized in table 1. Briefly CRS 1, there is no or minimal response of tumour(fig1) CRS 2, there is appreciable tumour response(fig2) and CRS 3, there is complete or near complete response with no residual tumour(fig3). Follow-up time was calculated from the date of first NACT to date of last follow-up. Date of recurrence and the vital status were also noted. For the purpose of analysis and ability to compare with previous data CRS1, CRS 2 were merged for comparison versus CRS3.overall survival was measured from the time of treatment to death or censored at last follow up. Progression free survival was calculated from the time of treatment administration to time at confirmed relapse or censored at last follow up. Survival outcomes were analysed and compared. Survival estimates were calculated by Kaplan-Meier method and cox proportional hazards regression was used to assess the association. Statistical significance was determined at a $P < .05$

Results

Among the high-grade serous adenocarcinoma, 24 cases received neo-adjuvant chemotherapy and underwent surgery and for which follow up was available. Age ranges from 30-75 with a median of 55 years. Most common clinical symptom was abdominal distension and mass per abdomen.

The median follow-up time was 23.5months (minimum: 6 months, maximum 5.0y.). All cases were treated with a minimum of 4 or 3 cycles with a base of carboplatin/paclitaxel neo-adjuvantly and a total of ≥6 cycles of chemotherapy.

There was evidence of significant association between age at diagnosis and overall survival (hazard ratio [HR]=1.10, 95% confidence interval [CI] :1.01-1.20, P=0.02) and with the progression free survival (hazard ratio [HR]=1.10, 95% confidence interval [CI] :1.01-1.30, P=0.03)

On histopathologic examination adnexal CRS scores were as follows. 15 cases showed complete or near complete response with no viable tumour CRS-3 (62.5%). 7 cases showed viable tumour which is irregularly distributed with appreciable tumour response CRS-2 (29.1) and 2 cases (8.33%) with CRS 1 score.

There was no evidence of association between overall survival and 2 tier omental CRS score (HR=0.22, 95%CI: 0.02-1.99, P=0.17 fig 4) or the progression free survival with the 2 -tier omental CRS score (HR=0.22, 95%CI :0.25-2.03, P=0.18 fig5).

There was no significant association between overall survival and the modified 2-tier adnexal score (HR=0.69, 95%CI :0.13-3.64, P=0.67 fig 6) or the

progression free survival with the 2-tier adnexal CRS score (HR=0.72, 95% CI :0.13-3.81, P=0.70 fig 7).

Discussion

The chemotherapy response score is used to score histopathologic response to neoadjuvant chemotherapy of patients with high-grade serous carcinoma. A 3-tier chemotherapy response score has been proposed, with the aim to identify patients at risk for recurrence and those at higher risk for mortality.

The CRS, when used on the omentum, has been shown to be reproducible and correlates with progression free survival.[9-10] And its correlation with overall survival has mixed results. CRS when used on the adnexa, there is also mixed results, ranging from no correlation to correlation with only PFS to correlation with PFS and OS[10,11].

Our study showed a CRS-1 score in 8.33% of cases, a CRS-2 score in 29.1% of cases and CRS-3 in 62.5% of cases. Our study showed no significant correlation of modified 2-tier omental CRS with the progression free survival or overall survival.

Previous studies Bohm et al [9,12] showed the omental 3-tier system to have a significant correlation with overall survival. And other studies like Ditzel et al[10] Singh et al[11] showed correlation with omental 2 tier CRS and PFS while showing no correlation with OS in 103 cases.

Recent study Barrett et al [20] had shown significant association between the PFS and modified 2-tier omental, modified 2-tier adnexal score and 3-tier adnexal score. And no significant association between the OS with the 3- tier score or the modified 2-tier omental and adnexal CRS score. Similar findings were noted with Michaan et al, which is that the CRS, when applied to the adnexa, had significant association with PFS but not OS. Other studies like Nath R et al also have shown no correlation including this study.

In addition CRS has shown some promise in identifying patients at risk for platinum-resistant disease (i.e, progression/recurrence within 6 months following platinum-based chemotherapy) [9,16]. Our study had one case of CRS2 which showed recurrence within 6 months of therapy and 3 cases (CRS2) presented with recurrence /progression in more than 6 months after therapy. Bohm et al in original development and validation of the CRS first noted the association between the omental CRS and platinum resistant disease which is also seen in other studies [9,16] Recent study Barrett et al [20] does not show significant association with platinum resistant disease and the omental CRS but does show significant association with the modified adnexal CRS and stated that adnexal CRS1/2 are more likely to develop platinum-resistant disease.

Although previous studies support the use of CRS as a prognostic indicator our study did not show a significant correlation between CRS and PFS or OS. The difference in the follow up time and the limited sample size may explain why we did not show significant correlation however additional extended follow up studies will be needed. Over all the chemotherapy response score a system for histopathologic assessment of response to neoadjuvant chemotherapy for high-grade serous carcinoma in ovary, fallopian tube or peritoneum is an easy, reproducible method for assessing the disease progression.

References

1. Siegel RL, Miller KD, Jemal A Cancer statistics. 2018 CA Cancer J Clin, 2018 Jan, 68(1):7-30

2. NIH National Cancer Institute SEER. http://seer.cancer.gov/statfactshtml/ovary.html
3. Kurman R.J, Shih le M 2010 The origin and pathogenesis of epithelial ovarian cancer: a proposed unifying theory *Am J Surg Pathol* 34: 433-443
4. Kindleberger D W, Lee Y, Miron A et al. 2007 intraepithelial carcinoma of the fimbria and pelvic serous carcinoma: evidence for a casual relationship *Am Surg Pathol* 31: 161-169
5. Kurman R.J, Carcingiu M.L, Herington C.S, Young R.H. (Eds): WHO Classification of tumours of Female Reproductive Organs (4th edition) IARC: Lyon 2014
6. Christopher D.M, Fletcher Diagnostic of Histopathology of tumors 4th Edition
7. Rubin SC, Benjamin I, Behbakht K et al, Clinical and pathological features of ovarian cancer in women with germline mutations of BRCA1. NEJM 1996;335:1413-1416
8. Vergote I,Trope CG, Amant F,et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. N Engl J Med.2010;363:943-953.
9. Bohm S, Faruqi a, Said , et al, Chemotherapy response score: development and validation of a system to quantify histopathologic response to neoadjuvant chemotherapy in tubo-ovarian high-grade serous carcinoma. J Clin Oncol.2015;33:2457-2463.
10. Ditzel HM, Strickland KC,Meserve EE,et al. Assessment of a chemotherapy response score (CRS) system for tubo-ovarian high -grade serous carcinoma (HGSC). *Int J Gynecol Pathol.2019*;38:230-240.
11. Singh P,Kaushal V,Rai B, et al. The chemotherapy response score is a useful histological predictor of prognosis in high-grade serous carcinoma. *Histopathology*.2018;72:619-625.
12. Bohm S, Le N ,Lockley M,et al. Histopathologic response to neoadjuvant chemotherapy as a prognostic biomarker in tubo-ovarian high -grade serous carcinoma: updated chemotherapy response score(CRS) results. *Int J Gynecol Cancer*.2019;29:353-356.
13. Coghlan E, Meniawy TM,MunroA,et al .Prognostic role of histological tumor regression in patients receiving neoadjuvant chemotherapy for high -grade serous tubo-ovarian carcinoma .*Int J Gynecol Cancer* .2071;27:708-713.
14. Michaan N ,Chong WY,Han NY ,et al. Prognostic value of pathologic chemotherapy response score in patients with ovarian cancer after neoadjuvant chemotherapy. *Int J gynecol cancer*.2018;28:1676-1682.
15. Lee JY,Chung YS, Na K,et al . External validation of chemotherapy response score system for histopathological assessment of tumour regression after neoadjuvant chemotherapy in tubo-ovarian high grade serous carcinoma. *J Gynecol Oncol*.2017; 28:e 73.
16. Rajkumar S,Polson A, Nath R,et al,Prognostic implications of histological tumor regression (Bohm score) in patients receiving neoadjuvant chemotherapy for high grade serous tubal and ovarian carcinoma. *Gynecol Oncol*.2018;151:264-268.
17. Prat J. Staging classification for cancer of the ovary, fallopian tube and peritoneum. *Int J. Gynaecol Obstet* 2014;124:1-5

18. Vang R, Shih Ie M, Kurman RJ. Ovarian low grade and high grade serous carcinoma: pathogenesis, clinicopathologic and molecular biologic features and diagnostic problems. *Adv Anat Pathol* 2009;16:267-82
19. Fleming ND ,Nick AM,Coleman RL,et al. Laparoscopic surgical algorithm to triage the timing of tumor reductive surgery in advanced ovarian cancer. *Obstet Gynecol*. 2018; 132: 54554
20. Barrett C.Lawson, Elizabeth, Roland L.Bassett ,et al. A 3-tier chemotherapy response score for ovarian/fallopian tube /peritoneal High grade serous carcinoma. Am J surg pathol 2020 ;44:2:p206-213.

Legend Table and Figure

Table 1: CRS Criteria

CRS1: No or minimal tumor response. Mainly tumor with no or minimal regression-associated fibroinflammatory changes, limited to a few foci; cases in which it is difficult to decide between regression and tumor-associated desmoplasia or inflammatory cell infiltration.
CRS 2: Appreciable tumor response, amid viable tumor that is readily identifiable. Tumor is regularly distributed, ranging from multifocal or diffuse regression-associated fibroinflammatory changes with viable tumor in sheets, streaks, or nodules to extensive regression-associated fibroinflammatory changes with multifocal residual tumor, which is easily identifiable
CRS 3: Complete or near-complete response with no residual tumor or minimal, irregularly scattered tumor foci seen as individual cells, cell groups or nodule up to 2mm maximum size. Mainly regression-associated fibroinflammatory changes or very little residual tumor in the complete absence of any inflammatory response

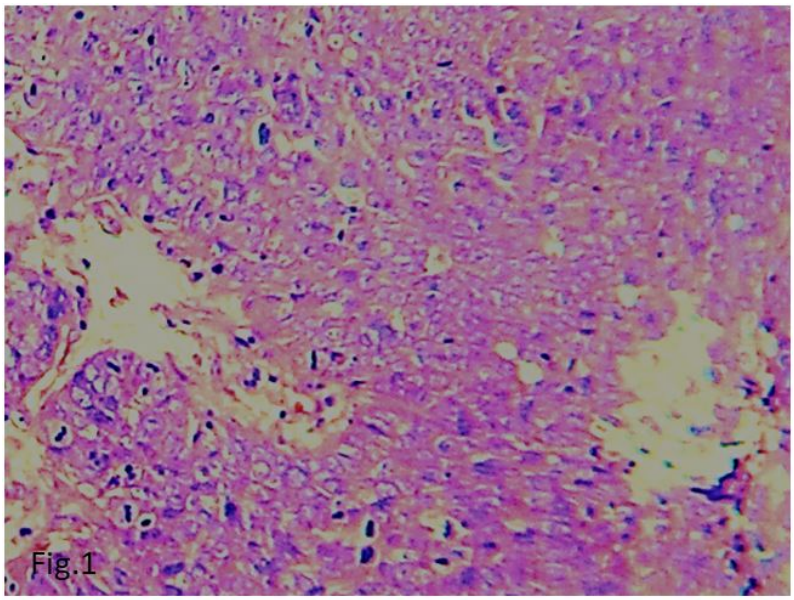

Fig.1

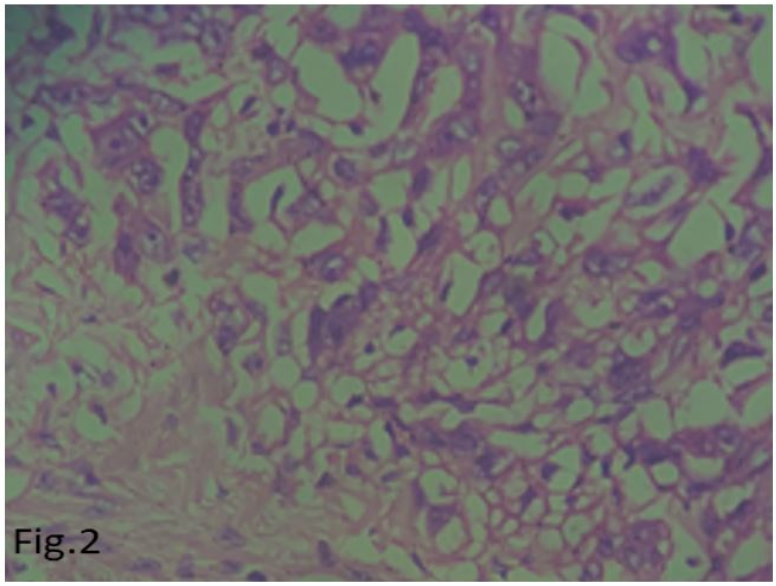

Fig.2

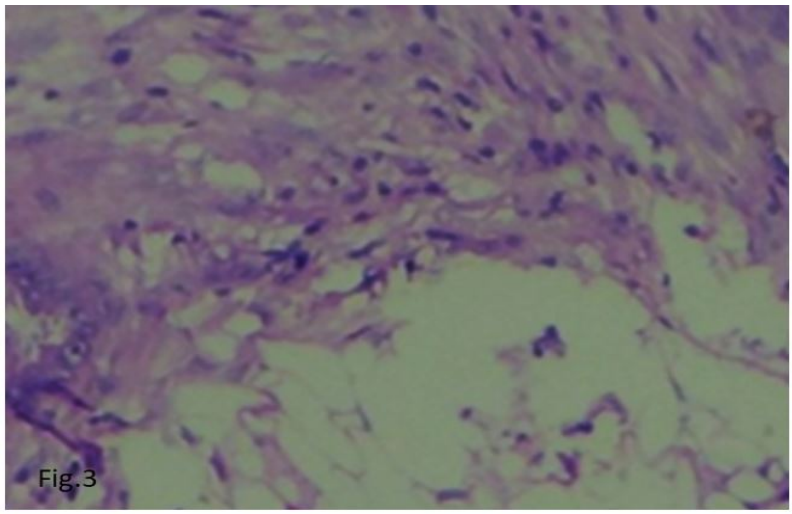

Fig.3

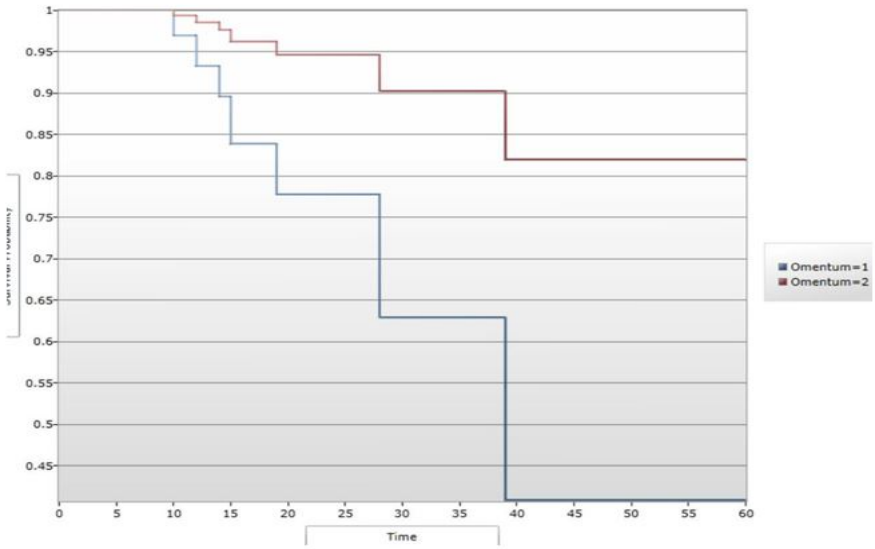

Fig 4. OS by modified omental 2-tier CRS

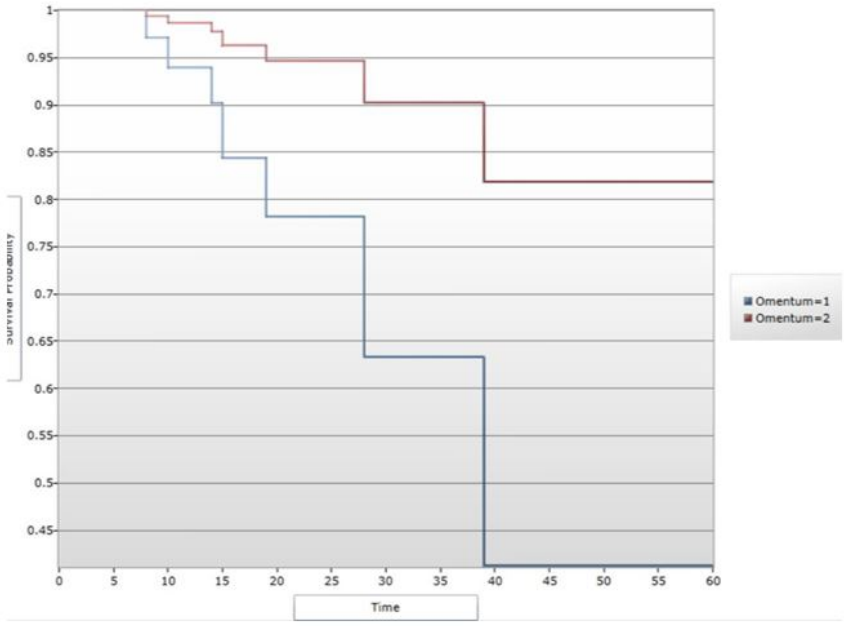

Fig 5 PFS by modified omental 2 tier CRS

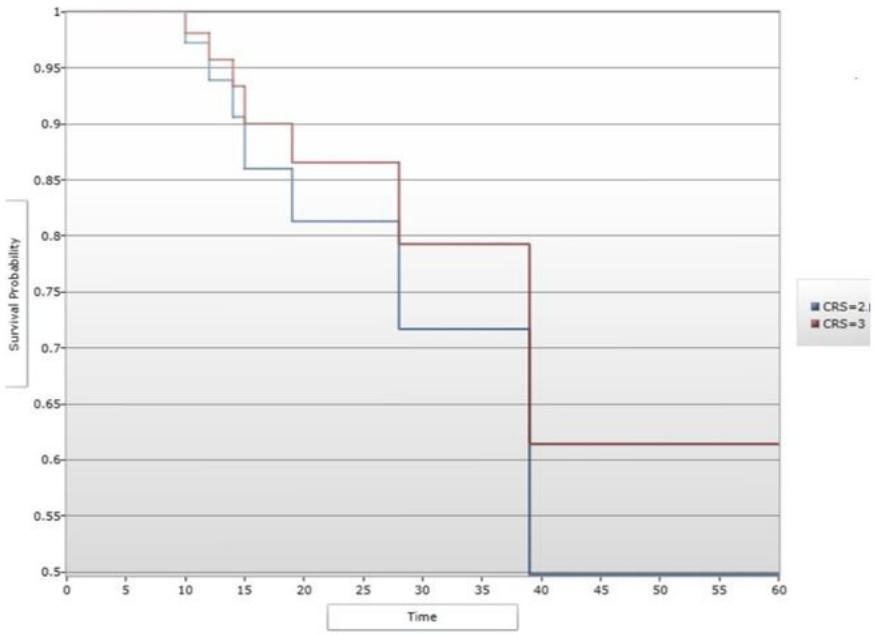

Fig 6: OS by modified adnexal 2 tier CRS

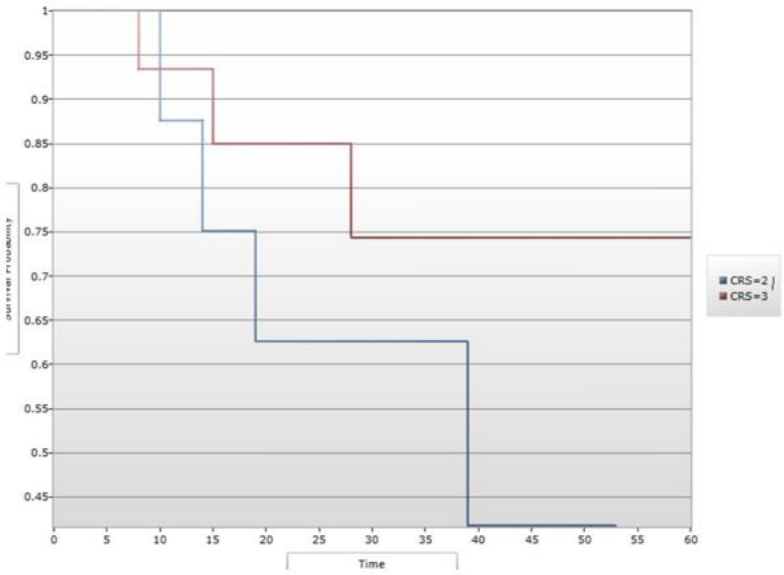

Fig 7: PFS by modified adnexal 2 tier CRS