Pengaruh mutasi patogenik BRCA1/2 tumor terhadap kesintasan pasien advanced stage-high grade serous Epithelial Ovarian Cancer di RSUPN Dr. Cipto Mangunkusumo, RSUP Persahabatan, dan RS MRCCC Siloam Jakarta = The Impact of pathogenic BRCA1/2 tumor mutation status on advanced Stage-High Grade serous Epithelial ovarian cancer survival Outcome at Dr. Cipto Mangunkusumo National Central Referral Hospital, Persahabatan Central Referral Hospital, and MRCCC Central R

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Abstrak

Tujuan: Mengetahui pengaruh mutasi patogenik BRCA1/2 tumor terhadap kesintasan pasien advanced stage-high grade serous epithelial ovarian cancer di RSUPN Dr. Cipto Mangunkusumo, RSUP Persahabatan, dan RS MRCCC Siloam Jakarta.
Metode: Sejumlah 68 sampel dari 144 pasien diagnosis high-grade serous epithelial ovarian cancer (HGSOC) stadium FIGO IIB-IV, periode 1 Januari 2015 sampai 31 Maret 2021, di RSUPN Dr. Cipto Mangunkusumo, RSUP Persahabatan, dan RS MRCCC Siloam Jakarta, menjalani pemeriksaan NGS mutasi patogenik BRCA1/2 tumor, dilibatkan dalam penelitian kohort historikal ini. Kami membandingkan karakteristik klinikopatologis pasien, dan hasil luaran kesintasan, setelah pasien menjalani tatalaksana primer, berdasarkan status mutasi patogenik BRCA1/2 tumor. Faktor terkait tatalaksana, yang diperkirakan berpengaruh terhadap hasil luaran kesintasan pasien, juga turut dianalisis dalam penelitian ini.
Hasil: Angka kejadian mutasi patogenik BRCA1/2 tumor diketahui sebesar 27,94% (19/68). Antara kelompok mutasi patogenik BRCA1/2 tumor, dengan kelompok tanpa mutasi patogenik, tidak terdapat perbedaan statistik signifikan berdasarkan usia, paritas, indeks massa tubuh (kg/m2), riwayat kanker payudara, stadium FIGO 2014, kadar CA125 serum pre operatif (U/mL), volume cairan ascites intra operatif (mL), lesi residual pasca laparotomi debulking, pemberian neoadjuvant chemotherapy (NACT), pemberian kemoterapi adjuvant. Riwayat kanker keluarga terkait HBOC, merupakan variabel paling berpengaruh terhadap mutasi patogenik BRCA1/2 tumor. Kelompok dengan riwayat kanker keluarga terkait HBOC, berisiko 5,212 kali lebih besar mengalami mutasi patogenik BRCA1/2 tumor, dibandingkan dengan kelompok tanpa riwayat kanker tersebut (RR adjusted 5,212; 95%CI 1,495-18,167; nilai p=0,010).
Pada kelompok mutasi patogenik BRCA1/2 tumor, kemungkinan meninggal 86% lebih rendah (RR adjusted 0,149; 95%CI 0,046-0,475; nilai p=0,001), dan median survival yang lebih baik (median 46 bulan; 95%CI 34,009-57,991; nilai p=0,001), apabila dibandingkan dengan kelompok tanpa mutasi patogenik (median 23 bulan; 95%CI 15,657-30,343; nilai p=0,001). Analisis multivariat menunjukkan mutasi patogenik BRCA1/2 tumor merupakan faktor prognostik independen yang baik terhadap hasil luaran kesintasan (RR adjusted 0,149; 95%CI 0,046-0,475; nilai p=0,001).
Kesimpulan: Pasien advanced stage-high grade serous epithelial ovarian cancer, dengan mutasi patogenik BRCA1/2 tumor, memiliki kesintasan lebih baik, dibandingkan pasien tanpa mutasi patogenik BRCA1/2 tumor.
.....Objective: To evaluate the impact of pathogenic BRCA1/2 tumor mutational status on advanced stage-

high grade serous epithelial ovarian cancer survival outcome at RSUPN Dr. Cipto Mangunkusumo, RSUP Persahabatan, and RS MRCCC Siloam Jakarta.
Methods: A total 68 of 144 patients diagnosed with FIGO 2014 stage IIB-IV high grade serous epithelial ovarian cancer (HGSOC) between January 1st, 2015 until March 31st, 2021, at RSUPN Dr. Cipto Mangunkusumo, RSUP Persahabatan, and RS MRCCC Siloam Jakarta, underwent NGS tumor BRCA1/2 gene testing, and were included in this cohort hystorical study. We compared patients clinicopathological characteristics, and survival outcomes after primary treatment, according to pathogenic BRCA1/2 tumor mutational status. Treatment-related factors that might affect patients' survival outcome were also investigated.
Results: The BRCA1/2 pathogenic tumor mutations prevalence was observed in this study 27.94% (19/68). There were no significant statistical differences in age, parity, body mass index (kg/m2), previous breast cancer history, FIGO 2014 staging, pre-operative serum CA 125 level (U/mL), intra operative ascites volume (mL), post cytoreductive surgery residual lesion, neoadjuvant chemotherapy (NACT), and adjuvant chemotherapy administration, between the pathogenic tumor BRCA1/2 mutation, and no pathogenic tumor BRCA1/2 mutation groups. The hereditary breast ovarian cancer family history (HBOC) variable has the strongest correlation with pathogenic tumor BRCA1/2 mutation. The group with a family history of HBOC-related cancer had a 5.212 times greater risk of developing pathogenic BRCA1/2 tumor mutations, compared with the group without a history of those cancer (RR adjusted 5.212; 95%CI 1.495-18.167; p value=0.010).
The pathogenic BRCA1/2 tumor mutation group displayed better survival outcome. In the pathogenic BRCA1/2 tumor mutation group, the likelihood of dying was 86% lower (RR adjusted 0.149; 95%CI 0.046-0.475; p-value=0.001), and the median survival was better (median 46 months; 95%CI 34.009- 57.991; p value=0.001), than without pathogenic BRCA1/2 tumor mutations group (median 23 months; 95%CI 15.657-30.343; p value=0.001). The multivariate analyses identified pathogenic BRCA1/2 tumor mutation as an independent favorable prognostic factor for survival outcome (RR adjusted 0.149; 95%CI 0.046-0.475; p-value=0.001).
Conclusions: In advanced stage-HGSOC, patients with pathogenic BRCA1/2 tumor mutations have a better prognosis with longer survival outcome than those without pathogenic BRCA1/2 tumor mutations.