

**KORELASI EKSPRESI
VEGF DAN MMP-9 DENGAN STADIUM T
KARSINOMA UROTHELIAL BULI**

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ABSTRAK

Latar Belakang: Karsinoma buli adalah kanker dengan angka kejadian terbanyak ke sepuluh di dunia dan kanker ke tujuh tersering pada pria. Karsinoma sel urothelial merupakan jenis kanker buli tersering, yaitu sebanyak 90-95%. Kedalaman invasi tumor merupakan faktor penting dalam prognosis dan terapi karsinoma urothelial. Ekspresi dari VEGF dan MMP-9 diperkirakan berhubungan dengan progresivitas dari karsinoma buli antara lain kedalaman invasi. VEGF dan reseptornya memiliki peran utama dalam proses angiogenesis yang merupakan peran penting dalam pertumbuhan tumor dan progresivitas dari karsinoma urothelial. *Matrix metalloproteinases 9* (MMP-9) memiliki peran penting pada beberapa proses perkembangan sel kanker seperti *remodeling* matriks ekstraseluler (ECM), angiogenesis, apoptosis dan proliferasi sel.

Tujuan: Menganalisis korelasi ekspresi VEGF dan MMP-9 pada berbagai stadium T karsinoma urothelial buli.

Metode: Penelitian observasional analitik dengan pendekatan *cross-sectional*. Sampel berasal dari 54 blok parafin dari sediaan *Radical Cystectomy* (RC) yang didiagnosis sebagai karsinoma urothelial buli di Laboratorium Patologi Anatomi RSUD Dr. Soetomo Surabaya periode 1 Januari 2010 – 31 Agustus 2019. Sampel penelitian dibagi berdasarkan stadium T, dan dilakukan pemeriksaan imunohistokimia menggunakan antibodi monoklonal VEGF dan MMP-9. Perbedaan ekspresi dari VEGF dan MMP-9 pada berbagai stadium T karsinoma urothelial akan dianalisis menggunakan *Kruskal-Wallis* dan *Anova test*, sedangkan korelasi antara VEGF dan MMP-9 pada berbagai stadium T karsinoma urothelial akan dianalisis menggunakan *Spearman test*.

Hasil: Tidak didapatkan perbedaan ekspresi VEGF pada berbagai stadium T karsinoma urothelial buli ($p > 0,05$). Didapatkan perbedaan ekspresi MMP-9 yang signifikan terhadap berbagai stadium T karsinoma urothelial buli ($p = 0,043$, $p < 0,05$). Didapatkan korelasi antara ekspresi VEGF dan MMP-9 pada berbagai stadium T karsinoma urothelial buli ($r_s = 0,50$, $p = 0,001$, $p < 0,05$).

Kesimpulan: Penelitian ini menunjukkan bahwa ekspresi MMP-9 dapat berbeda tergantung pada kedalaman invasi tumor pada karsinoma urothelial buli. Didapatkannya korelasi antara VEGF dan MMP-9 menunjukkan bahwa VEGF dan MMP-9 memiliki peran penting pada invasi karsinoma urothelial buli.

Kata kunci: karsinoma urothelial, VEGF, MMP-9, Stadium T.

**CORELATION OF
VEGF AND MMP-9 EXPRESSION
IN T STAGE OF BLADDER UROTHELIAL CARCINOMA**

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ABSTRACT

Background: Bladder cancer is the tenth-most common cancer in worldwide and the seventh-most common malignancy in men. The majority, 90–95%, of the bladder carcinomas are urothelial carcinomas. The depth of invasion plays important role in the prognostic and therapeutic factor in urothelial carcinomas. The expression of VEGF and MMP-9 may associated with the progression of bladder carcinoma, such as depth of invasion. VEGF and its receptors play a central role in the process of angiogenesis which is an important role in tumor growth and progression of urothelial carcinoma. Matrix metalloproteinases (MMPs) have important roles in several cancer-supporting cellular processes, such as extracellular matrix (ECM) remodeling, angiogenesis, apoptosis, epithelial-to-mesenchymal transition and cell proliferation.

Objective: To analyze the corelation of VEGF and MMP-9 expression in various T stage of bladder urothelial carcinoma.

Methods: An analytical observational research with cross-sectional were conducted on 54 formalin fixed paraffin-embedded tissue from Radical Cystectomy (RC) which were diagnosed as bladder urothelial carcinoma at the Anatomical Pathology Laboratory of Dr. Soetomo General Hospital Surabaya during January 2010 - 31 August 2019. The samples of bladder urothelial carcinoma were divided based on the T stage and immunostained using VEGF and MMP-9 monoclonal antibodies. The difference of VEGF and MMP-9 expression in T stage of bladder urothelial carcinoma were analysed using Kruskal-Wallis and Anova test, the correlation between VEGF and MMP-9 expression in various T stage of bladder urothelial carcinoma were analysed using Spearman test.

Result: This study showed no difference significancy of VEGF expression in T stage of bladder urothelial carcinoma ($p > 0,05$) but there were difference significancy of MMP-9 expression in T stage of bladder urothelial carcinoma ($p = 0,043$, $p < 0,05$). There was a correlation between VEGF and MMP-9 in various T stage of bladder urothelial carcinoma ($r_s = 0,50$, $p = 0,001$, $p < 0,05$).

Conclucion: MMP-9 expression is different based on the depth invasion in bladder urothelial carcinoma. The correlation between VEGF and MMP-9 expression in bladder urothelial carcinoma may play a role in tumor invasion.

Keywords: urothelial carcinoma, VEGF, MMP-9, T stage