

# DISERTASI

HUBUNGAN EKSPRESI TRANSFORMING GROWTH FACTOR  $\beta 1$ , MATRIX METALLOPROTEINASE-1,  
TISSUE INHIBITOR MATRIX METALLOPROTEINASE-3 DENGAN KEPADATAN FIBROSIS  
PASCA TRANSURETHRAL RESECTION OF PROSTATE



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## ABSTRAK

### HUBUNGAN EKSPRESI TRANSFORMING GROWTH FACTOR $\beta 1$ , MATRIX METALLOPROTEINASE-1, TISSUE INHIBITOR MATRIX METALLOPROTEINASE-3 DENGAN KEPADATAN FIBROSIS PASCA TRANSURETHRAL RESECTION OF PROSTATE

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*Bladder neck contracture* (BNC) adalah salah satu komplikasi *Transurethral Resection Of Prostate* (TURP). Sampai saat ini belum ada kejelasan pathogenesis BNC. BNC adalah fibrosis pada *bed* bekas kerokan prostat. *TGF $\beta 1$*  merupakan *growth factory* yang berperan pada fibrosis berbagai organ. Jika BNC adalah fibrosis pada fase remodelling penyembuhan luka maka MMPs dan TIMPs akan berperan karena menentukan hasil akhir degradasi matrix ekstra seluler pada jaringan luka. MMP-1 dan TIMP-3 diketahui berperan dalam fase tersebut. Penelitian ini bertujuan untuk membuktikan hubungan *TGF $\beta 1$* , MMP-1 dan TIMP-3 dengan kepadatan fibrosis pasca TURP.

Penelitian ini merupakan penelitian observasional dengan desain *cross sectional*. Sebanyak 20 pasien yang dioperasi ulang akibat BNC diambil sebagai sampel. Jaringan fibrosis (BNC) lalu diperiksa secara mikroskopik dengan pewarnaan HE untuk menentukan kepadatan fibrosisnya dengan menghitung rata-rata jaringan fibrosis dari 4 lapang pandang yang berbeda. Pada jaringan tersebut juga dilakukan pemeriksaan immunohistokimia (IHK) untuk menentukan persentase ekspresi *TGF- $\beta 1$* , MMP-1 dan TIMP-3. Untuk mengetahui hubungan ekspresi *TGF- $\beta 1$* , MMP-1 dan TIMP-3 dengan kepadatan fibrosis dilakukan uji korelasi pearson.

Penelitian ini mendapatkan kepadatan rata-rata fibrosis  $74,31 \% \pm 15\%$ . Dari hasil pemeriksaan IHK didapatkan rata-rata ekspresi *TGF- $\beta 1$*   $51\% \pm 13,49\%$ , sedangkan MMP-1  $27,50 \% \pm 15,67\%$  dan TIMP-3  $24,94\% \pm 17,33\%$ . Dari hasil uji korelasi *TGF- $\beta 1$*  dengan kepadatan fibrosis didapatkan makin tinggi ekspresi *TGF- $\beta 1$*  makin kurang kepadatan fibrosis dengan korelasi yang lemah ( $r=0,27$ ), secara statistik korelasi keduanya tidak bermakna ( $p>0,05$ ). Sedangkan untuk MMP-1 didapatkan semakin tinggi ekspresi MMP-1, makin bertambah kepadatan fibrosis dengan korelasi yang lemah ( $r=0,25$ ), secara statistik korelasi keduanya tidak bermakna ( $p>0,05$ ). Sedangkan dengan TIMP-3 didapatkan makin tinggi ekspresi TIMP-3, makin bertambah kepadatan fibrosis dengan korelasi sedang ( $r=0,5$ ), secara statistik korelasi keduanya bermakna ( $p<0,05$ ).

Dari penelitian ini disimpulkan bahwa TIMP-3 merupakan faktor yang berperan dalam patogenesis BNC pasca TURP.

Kata kunci: *Bladder neck contracture*, *TGF- $\beta 1$* , MMP-1 dan TIMP-3.

## ABSTRACT

### CORRELATION OF TRANSFORMING GROWTH FACTOR $\beta$ 1, MATRIX METALLOPROTEINASE-1, TISSUE INHIBITOR MATRIX METALLOPROTEINASE-3 WITH DENSITY OF FIBROSIS IN POST-TRANSURETHRAL RESECTION OF PROSTATE

Etriyel Myh

Bladder neck contracture (BNC) is one of the most common complications of TURP. However, currently, there is no clear description of BNC pathogenesis available. BNC is a fibrosis disease occurring in the remodelling phase of wound healing process, which involves growth factor, matrix metalloproteinase (MMPs) and tissue inhibitory matrix metalloproteinases (TIMPs). TGF- $\beta$ 1 is a growth factor that plays a role in various organ fibrosis, whereas MMP-1 and TIMP-3 are known to play role in extracellular matrix degradation at the remodelling phase of wound healing process. This study aims to prove the relationship of TGF  $\beta$ 1, MMP-1 and TIMP-3 with tissue fibrosis density post-TURP.

This research was an observational research with cross sectional design. A total of 20 samples from post-TURP patients who underwent re-operation due to BNC were included. The fibrosis tissue (BNC) were resected and examined microscopically after HE staining to determine the density of fibrosis. Immunohistochemistry (IHC) examination was also performed to determine the expression of TGF  $\beta$ 1, MMP-1 and TIMP-3. Correlation of TGF  $\beta$ 1, MMP-1 and MP3 with fibrosis density was measured using Pearson correlation test.

This study obtained an average density of fibrosis of 74.31%  $\pm$  15% in the resected tissue. IHC examination obtained average expression of TGF $\beta$ -1 51%  $\pm$  13.49%, while MMP-1 27.50%  $\pm$  15.67% and TIMP-3 24.94%  $\pm$  17.33%. Correlations between TGF $\beta$ 1, MMP-1 and TIMP-3 with the density of fibrosis were measured using Pearson correlation test. TGF $\beta$ -1 had a weak ( $r = 0.27$ ) negative correlation to fibrosis density; the higher the TGF $\beta$ -1 expression, the less density of fibrosis were observed. The correlation was not statistically significant ( $p > 0,05$ ). Higher expression of MMP-1 correlated weakly ( $r = 0.25$ ) to more fibrosis density. Again, this correlation was not found to be statistically significant ( $p > 0.05$ ). Expression of TIMP-3 correlated positively and significantly with fibrosis density. The correlation observed was moderate ( $r = 0.5$ ) and statistically significant ( $p < 0.05$ ).

From this research it can be concluded that TIMP-3 is a factor that plays an important role in the pathogenesis of BNC post TURP.

Keywords: Bladder neck contracture, TGF- $\beta$ 1, MMP-1 and TIMP-3

