

Infiltrating Tumor Border Configuration is a Poor Prognostic Factor in Stage II and III Colon Adenocarcinoma

Yasmeen Z. Qwaider, MD , Naomi M. Sell, MD, MHS , Caitlin E. Stafford, BA , Hiroko Kunitake, MD, MPH , James C. Cusack, MD , Rocco Ricciardi, MD, MPH , Liliana G. Bordeianou, MD , Vikram Deshpande, MD, PhD , Robert N. Goldstone, MD , Christy E. Cauley, MD, MPH , and David L. Berger, MD

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要旨： Tumor border configuration (TBC)は、大腸癌の予後因子とされているが、その意義は十分に明らかになっていない。また、術後補助化学療法が推奨となる Stage II high risk 症例については未だに議論が行われている。

筆者らはステージ II および III 大腸癌において、TBC が OS および DFS に及ぼす影響について検討した。2004～2015 年に根治手術が行われた大腸癌 700 例(II 期 371 例、III 期 329 例)を対象とし、TBC は”Infiltrating TBC”と、”Pushing TBC”に分類した。(Figure 1.)
ステージを調整せずに Infiltrating TBC と、Pushing TBC に 2 群に分類した Kaplan-Meier 曲線では、Infiltrating TBC が OS ($p=0.0026$)、DFS ($p=0.0079$) とともに有意に予後不良であった。(Figure 2.)

また、ステージと TBC のタイプで 4 群に分類すると、Stage III の Infiltrating TBC は、OS ($p=0.004$)、DFS ($p=0.02$)とともに他のグループと比較し有意に不良であった。(Figure 3.)
すべての交絡因子を調整し多変量解析行くと、Infiltrating TBC は Pushing TBC と比較し OS、DFS とともに有意に不良であった。(Table 3.)

さらに、Stage II の Infiltrating TBC と Stage III の Pushing TBC の OS のハザード比はグループ間のペアワイズ比較検定を行っても有意差はみられなかった。DFS についても同様の結果であった。

Take home message

- (1)TBC は”Infiltrating TBC”と”Pushing TBC”に分類され、比較的簡便に評価でき観察者間の一致率は高い。
- (2)Infiltrating TBC は Stage II および III の大腸癌の予後不良因子である。
- (3)Stage II で Infiltrating TBC の症例は術後補助化学療法を考慮すべきである。

査読者 橋元 麻生

Figure 1. Colon adenocarcinoma.

A Infiltrating tumor border configuration, B pushing tumor border configuration. Scan bar: 20 μ m

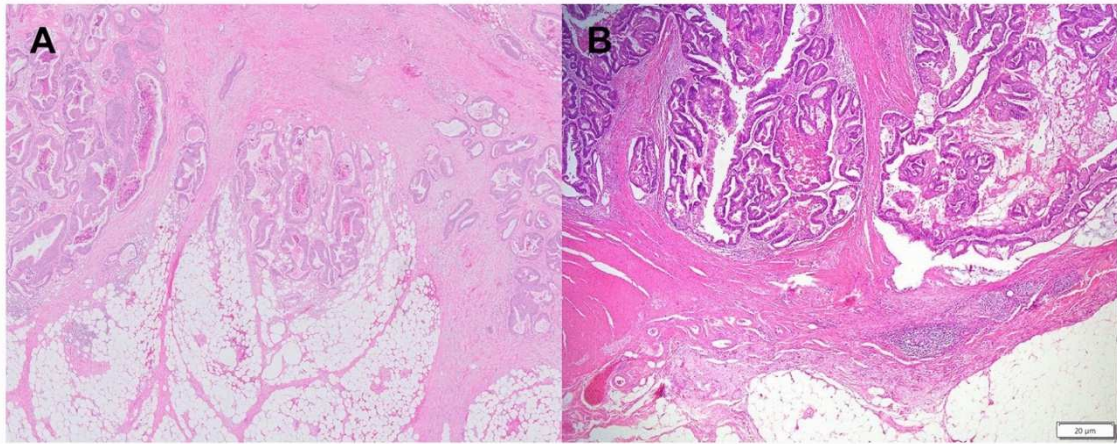


Table 1. Demographics for patients with stage II disease ($N = 371$)

| Characteristics | Total [$N = 371$] (%) | Tumor border configuration | | p value |
|-----------------------|-------------------------|--------------------------------|---------------------------|-----------|
| | | Infiltrating [$n = 218$] (%) | Pushing [$n = 153$] (%) | |
| Age | 68 \pm 15 | 69 \pm 15 | 70 \pm 15 | 0.5 |
| Sex | | | | 1 |
| Female | 198 (53) | 116 (53) | 82 (53) | |
| Male | 173 (47) | 102 (47) | 71 (47) | |
| Adjuvant chemotherapy | | | | 0.06 |
| Received | 61 (16) | 43 (20) | 18 (12) | |
| Did not receive | 310 (84) | 175 (80) | 135 (88) | |
| Extent of invasion | | | | 0.07 |
| T3 | 292 (79) | 164 (75) | 128 (84) | |
| T4 | 79 (21) | 54 (25) | 25 (16) | |
| Histologic grade | | | | 0.2 |
| Low | 312 (84) | 189 (87) | 123 (80) | |
| Intermediate | 5 (1) | 2 (1) | 3 (2) | |
| High | 54 (15) | 26 (12) | 28 (18) | |
| Anatomic site | | | | 0.4 |
| Right colon | 212 (57) | 118 (54) | 94 (61) | |
| Left colon | 110 (30) | 69 (32) | 41 (27) | |
| Transverse colon | 49 (13) | 31 (14) | 18 (12) | |

Table 2. Demographics for patients with stage III disease ($N = 329$)

| Characteristics | Total [$N = 329$] | Tumor border configuration | | p value |
|-----------------------|---------------------|--------------------------------|--------------------------|-----------|
| | | Infiltrating [$n = 248$] (%) | Pushing [$n = 81$] (%) | |
| Age | 67 ± 15 | 65 ± 15 | 71 ± 15 | < 0.001 |
| Sex | | | | 0.5 |
| Female | 170 (52) | 125 (50) | 45 (56) | |
| Male | 159 (48) | 123 (50) | 36 (44) | |
| Adjuvant chemotherapy | | | | 0.08 |
| Received | 238 (72) | 186 (75) | 52 (64) | |
| Did not receive | 91 (28) | 62 (25) | 29 (36) | |
| Extent of invasion | | | | < 0.001 |
| T1 | 12 (4) | 8 (3) | 4 (5) | |
| T2 | 27 (8) | 12 (5) | 15 (19) | |
| T3 | 193 (59) | 141 (57) | 52 (64) | |
| T4 | 97 (29) | 87 (35) | 10 (12) | |
| Histologic grade | | | | 1 |
| Low | 235 (72) | 177 (71) | 58 (72) | |
| Intermediate | 11 (3) | 9 (4) | 2 (2) | |
| High | 83 (25) | 62 (25) | 21 (26) | |
| Anatomic site | | | | 0.1 |
| Right colon | 186 (57) | 134 (54) | 52 (64) | |
| Left colon | 124 (38) | 101 (41) | 23 (28) | |
| Transverse colon | 19 (6) | 13 (5) | 6 (8) | |

Figure 2. Kaplan-Meier curves for overall and disease-free survival between infiltrating and pushing TBCs. *TBC* tumor border configuration

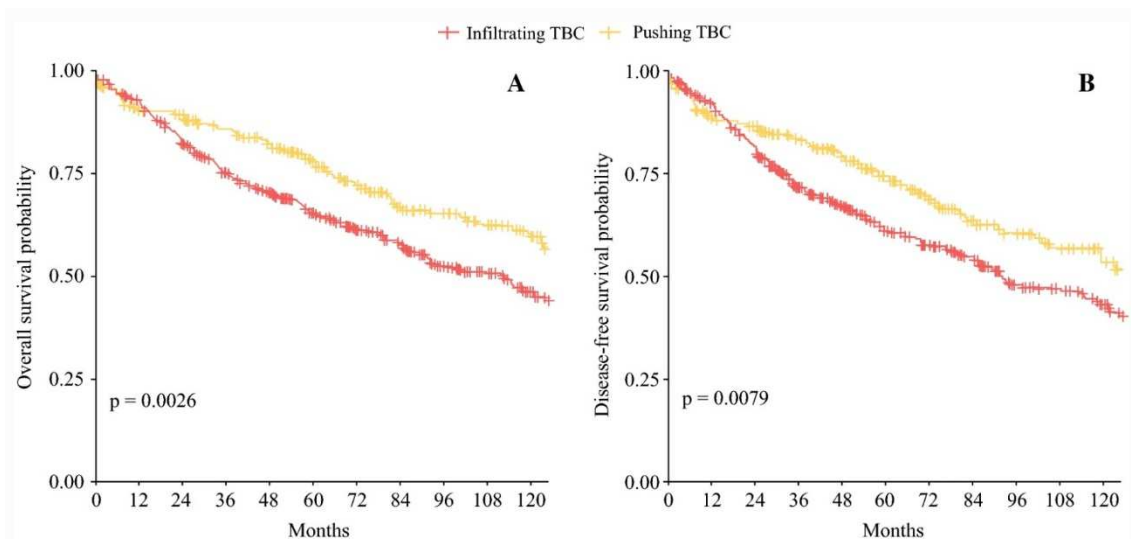


Figure 3. Kaplan-Meier curves for overall and disease-free survival between groups.

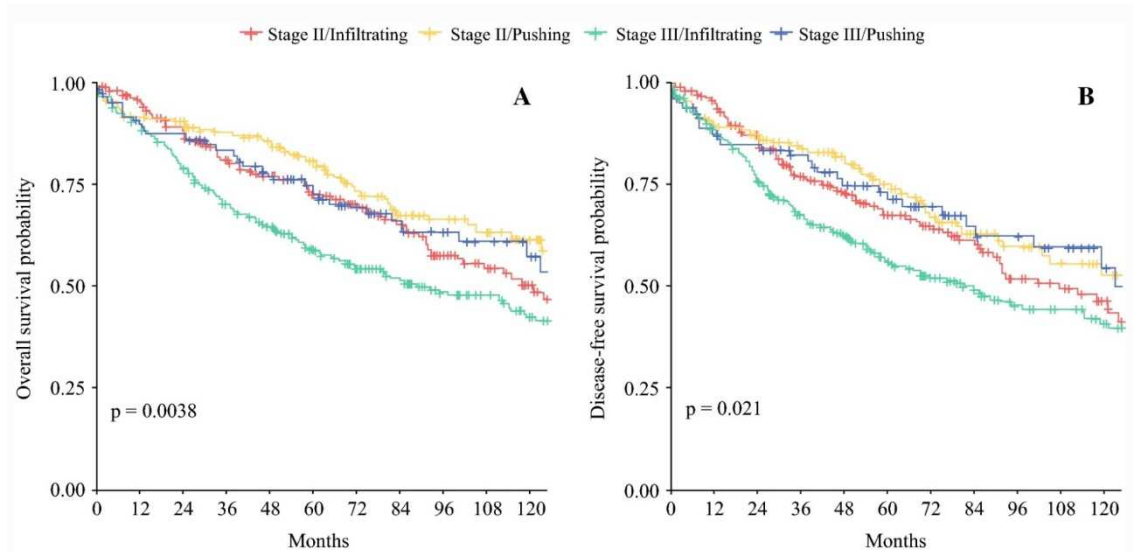


Table 3. Multivariable Cox regression model for overall and disease-free survival ($N = 700$)

| Characteristics | Overall survival | | Disease-free survival | |
|----------------------------|---------------------------|----------------|---------------------------|----------------|
| | aHR ^a (95% CI) | <i>p</i> value | aHR ^a (95% CI) | <i>p</i> value |
| Age | 1.0 (1.0–1.1) | < 0.001 | 1.0 (1.0–1.1) | < 0.001 |
| ASA | 1.8 (1.5–2.2) | < 0.001 | 1.7 (1.4–2.1) | < 0.001 |
| Adjuvant chemotherapy | 0.6 (0.5–0.9) | 0.01 | 0.6 (0.4–0.8) | 0.003 |
| EMVI | 1.8 (1.4–2.3) | < 0.001 | 1.7 (1.1–1.9) | < 0.001 |
| Tumor border configuration | | | | |
| Pushing | Reference | | Reference | |
| Infiltrating | 1.8 (1.4–2.4) | < 0.001 | 1.7 (1.3–2.2) | < 0.001 |
| Stage | | | | |
| II | Reference | | Reference | |
| III | 1.5 (1.1–2.0) | 0.01 | 1.4 (1.0–1.9) | 0.03 |
| Histologic grade | | | | |
| Low | Reference | | Reference | |
| Intermediate | 0.9 (0.4–2.3) | 0.8 | 0.8 (0.3–2.0) | 0.8 |
| High | 1.4 (1.1–1.9) | 0.01 | 1.6 (1.2–2.1) | 0.003 |
| Anatomic site | | | | |
| Right colon | Reference | | Reference | |
| Left colon | 1.2 (0.9–1.6) | 0.2 | 1.3 (1.0–1.7) | 0.1 |
| Transverse colon | 1.2 (0.7–1.8) | 0.5 | 1.3 (0.9–2.0) | 0.2 |

aHR adjusted hazard ratio, CI confidence interval, ASA American Society of Anesthesiologists, EMVI extramural vascular invasion

^aAll variables were adjusted for age, histologic grade, stage, anatomic site, adjuvant chemotherapy, EMVI, and ASA score