**Section 1- study period of 1995 - 2000 vs. 2005 -2010**

**Table 1 summary statistics for continuous variables**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| variable | Summary stats | 1995- 2000 (N=85) | 2005 – 2010(N=114) | p-value |
| AGE |  |  |  | 0.44 |
|  | n | 85 | 114 |  |
|  | mean | 35.88  | 34.41 |  |
|  | Standard deviation | 12.12  | 13.86 |  |
|  | median | 33 | 31.50 |  |
|  | IQR-[Q1, Q3] | [26.0, 43.0] | [24.0, 40.0] |  |
|  | [min, max] | [18.0, 66.0] | [14.0, 86.0] |  |
|  |  |  |  |  |
| Time from DX to surgery (month) |  |  |  | 0.71  |
|  | n | 81 | 114 |  |
|  | mean | 94.37  | 91.46 |  |
|  | Standard deviation | 83.82  | 89.46  |  |
|  | median | 72 | 72 |  |
|  | IQR-[Q1, Q3] | [24.0, 168.0] | [24.0, 132.0] |  |
|  | [min, max] | [0.0, 408.0] | [0.0, 468.0] |  |
|  |  |  |  |  |
| Length of stay (LOS-days) |  |  |  | 0.05  |
|  | n | 85 | 114 |  |
|  | mean | 16.87  | 12.32  |  |
|  | Standard deviation | 16.68  | 8.00 |  |
|  | median | 10 | 9 |  |
|  | IQR-[Q1, Q3] | [8.0, 21.0] | [7.0, 17.0] |  |
|  | [min, max] | [5.0, 89.0] | [4.0, 38.0] |  |
|  |  |  |  |  |
| Small bowl resected (cm) |  |  |  | 0.82 |
|  | n | 59 | 91 |  |
|  | mean | 24.64 | 26.12 |  |
|  | Standard deviation | 12.56 | 17.49 |  |
|  | median | 21 | 23 |  |
|  | IQR-[Q1, Q3] | [15.0, 31.0] | [14.0, 34.0] |  |
|  | [min, max] | [7.0, 56.0] | [5.0, 130.0] |  |

**Table 2 time from Dx to surgery in three groups – summary stats**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Time from DX to surgery (month) | Summary stats | 1995- 2000 (N=85) | 2005 – 2010 –NON-anti-TNF(N=76) | 2005 – 2010 anti-TNF(N=38) | p-value |
|  |  |  |  |  | 0.09 |
|  | n | 81 | 76 | 38 |  |
|  | mean | 94.37  | 87.26  | 99.84  |  |
|  | Standard deviation | 83.82  | 100.22 | 63.06  |  |
|  | median | 72 | 48 | 90 |  |
|  | IQR-[Q1, Q3] | [24.0, 168.0] | [15.0, 120.0] | [60.0, 132.0] |  |
|  | [min, max] | [0.0, 408.0] | [0.0, 468.0] | [12.0, 252.0] |  |

**Table 3 summary statistics for categorical variables**

| **Variables** | **Category** | **Total** | **1995-2000 (N=85)% (n)** | **2005-2010****(N=114)% (n)** | **p-value(2-sided)** |
| --- | --- | --- | --- | --- | --- |
| GENDER | M | 88 | 30.6(26) | 54.4(62) | 0.001 |
|  | F | 111 | 69.4(59) | 45.6(52) |  |
| AGE AT DX | A1 (<16) | 32 | 9.8(8) | 21.1(24) | 0.11 |
|  | A2(17-40) | 136 | 74.4(61) | 65.8(75) |  |
|  | A3 (>40) | 28 | 15.9(13) | 13.2(15) |  |
| DISEASE BEHAVIOR | B1 (inflame) | 47 | 38.8(33) | 12.3(14) | <0.0001 |
|  | B2(stricture) | 79 | 31.8(27) | 45.6(52) |  |
|  | B3(penetrate) | 73 | 29.4(25) | 42.1(48) |  |
| DISEASE LOCATION | L1 (lleal) | 58 | 32.9(28) | 26.3(30) | 0.01 |
|  | L2(Colonic) | 41 | 28.2(24) | 14.9(17) |  |
|  | L3(lleocolonic) | 100 | 38.8(33) | 58.8(67) |  |
| USE OF ANTI-TNF | Y | 38 | 0(0) | 33.3(38) | <0.0001 |
|  | N | 161 | 100(85) | 66.7(76) |  |
| USE CS | Y | 144 | 69.1(58) | 75.4(86) | 0.32 |
|  | N | 54 | 31(26) | 24.6(28) |  |
| USE 5ASA | Y | 79 | 53.6(45) | 29.8(34) | 0.001 |
|  | N | 119 | 46.4(39) | 70.2(80) |  |
| USE IM | Y | 82 | 21.4(18) | 56.1(64) | <0.0001 |
|  | N | 116 | 78.6(66) | 43.9(50) |  |
| POST OP COMPLICATION | Y | 18 | 9.4(8) | 8.8(10) | 0.88 |
|  | N | 181 | 90.6(77) | 91.2(104) |  |

**Section 2 – on anti-TNF patients vs. non anti-TNF patients (cohort 2005-2010)**

**Table 1 summary statistics for continuous variables**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **variable** | **Summary stats** | **anti-TNF= NO (N=76)** | **anti-TNF= YES****(N=38)** | **p-value** |
| AGE |  |  |  | 0.10 |
|  | n | 76 | 38 |  |
|  | mean | 35.93 | 31.37 |  |
|  | Standard deviation | 14.05 | 13.14 |  |
|  | median | 33.5 | 29.5 |  |
|  | IQR-[Q1, Q3] | [26.0, 44.0] | [23.0, 35.0] |  |
|  | [min, max] | [17.0, 86.0] | [14.0, 70.0] |  |
|  |  |  |  |  |
| Time from DX to surgery (month) |  |  |  | 0.02 |
|  | n | 76 | 38 |  |
|  | mean | 87.26  | 99.84  |  |
|  | Standard deviation | 100.22 | 63.06  |  |
|  | median | 48 | 90 |  |
|  | IQR-[Q1, Q3] | [15.0, 120.0] | [60.0, 132.0] |  |
|  | [min, max] | [0.0, 468.0] | [12.0, 252.0] |  |
|  |  |  |  |  |
| Length of stay (LOS-days) |  |  |  | 0.76 |
|  | n | 76 | 38 |  |
|  | mean | 12.25 | 12.47  |  |
|  | Standard deviation | 7.73 | 8.63 |  |
|  | median | 10 | 9 |  |
|  | IQR-[Q1, Q3] | [7.0, 16.5] | [6.0, 19.0] |  |
|  | [min, max] | [4.0, 34.0] | [4.0, 38.0] |  |
|  |  |  |  |  |
| Small bowl resected (cm) |  |  |  | 0.92 |
|  | n | 64 | 27 |  |
|  | mean | 26.84  | 24.41 |  |
|  | Standard deviation | 19.28 | 12.43 |  |
|  | median | 21.5 | 23 |  |
|  | IQR-[Q1, Q3] | [15.0, 31.5] | [14.0, 36.0] |  |
|  | [min, max] | [5.0, 130.0] | [5.0, 47.0] |  |

**Table 2 summary statistics for categorical variables**

| **variables** | **Category** | **Total** | **Anti-TNF = ‘NO’ (N=76)% (n)** | **Anti-TNF = ‘Yes’ (N=38)% (n)** | **p-value(2-sided)** |
| --- | --- | --- | --- | --- | --- |
| GENDER | M | 62 | 51.3(39) | 60.5(23) | 0.35 |
|  | F | 52 | 48.7(37) | 39.5(15) |  |
| AGE AT DX | A1 (<16) | 24 | 11.8(9) | 39.5(15) | 0.003 |
|  | A2(17-40) | 75 | 73.7(56) | 50(19) |  |
|  | A3 (>40) | 15 | 14.5(11) | 10.5(4) |  |
| DISEASE BEHAVIOR | B1 (inflame) | 14 | 9.2(7) | 18.4(7) | 0.33 |
|  | B2(stricture) | 52 | 48.7(37) | 39.5(15) |  |
|  | B3(penetrate) | 48 | 42.1(32) | 42.1(16) |  |
| DISEASE LOCATION | L1 (lleal) | 30 | 27.6(21) | 23.7(9) | 0.01 |
|  | L2(Colonic) | 17 | 7.9(6) | 29(11) |  |
|  | L3(lleocolonic) | 67 | 64.5(49) | 47.4(18) |  |
| USE CS | Y | 86 | 72.4(55) | 81.6(31) | 0.28 |
|  | N | 28 | 27.6(21) | 18.4(7) |  |
| USE 5ASA | Y | 34 | 30.3(23) | 29(11) | 0.88 |
|  | N | 80 | 69.7(53) | 71.1(27) |  |
| USE IM | Y | 64 | 44.7(34) | 79(30) | 0.001 |
|  | N | 50 | 55.3(42) | 21.1(8) |  |
| POST OP COMPLICATION | Y | 10 | 6.6(5) | 13.2(5) | 0.30 |
|  | N | 104 | 93.4(71) | 86.8(33) |  |

**Summary statistics of time from date of disease diagnosis to surgery for the four groups in the 2005 - 2010 cohort:**

A: patients with anti-TNF only

B: patients with anti-TNF and Immunomodulators (IM)

C: patients with immunomodulators (IM) only

D: patients with neither anti-TNF or immunomodulators (IM)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **variable** | **Summary stats** | **A** **(N=8)** | **B****(N=30)** | **C****(N=34)** | **D****(N=42)** |
| AGE | No of missing | 0 | 0 | 0 | 0 |
|  | mean | 61.50 | 110.07 | 76.38 | 96.07 |
|  | Standard deviation | 38.18 | 64.87 | 69.81 | 119.46 |
|  | median | 60.00 | 96.00 | 54.00 | 36.00 |
|  | IQR-[Q1, Q3] | [24.00, 90.00] | [72.00, 156.00] | [24.00, 108.00] | [12.00, 144.00] |
|  | [min, max] | [24.00, 120.00] | [12.00, 252.00] | [5.00, 300.00] | [0.00, 468.00] |

Comparison among the groups:

|  |  |
| --- | --- |
| **variable** | **p-value** |
| All 4 groups | 0.06 |
| A vs. B | 0.05 |
| A vs. C | 0.97 |
| A, B,C | 0.03 |
| B vs. C | 0.02 |

**Cox model for time to surgery:**

To examine the effect of anti-TNF on the time from diagnosis to surgery, we performed a multivariable cox proportional hazard model. Since majority of patients started anti-TNF medication during the follow-up period, anti-TNF use was parameterized as a time-dependent variable in the analysis. The model was adjusted for preselected confounding variables, including age, gender, smoking status, disease location and disease behavior and use of IM.

**Summary results of Cox proportional hazard model:**

|  |  |  |  |
| --- | --- | --- | --- |
| **variable** | **Hazard ratio**  | **95% Confidence interval**  | **p-value** |
| **Lower limit** | **Upper limit** |
| Anti-TNF (yes vs. no) | 3.57 | 1.98 | 6.44 | <0.0001 |
| Gender (Male vs. Female) | 1.16 | 0.73 | 1.85 | 0.52 |
| Age at Dx (A2 vs. A1) | 2.30 | 1.27 | 4.17 | 0.01 |
|  (A3 vs. A1) | 2.80 | 1.13 | 6.93 | 0.03 |
| Disease location (L2 vs. L1) | 0.73 | 0.27 | 1.94 | 0.52 |
|  (L3 vs. L1) | 1.49 | 0.84 | 2.63 | 0.17 |
| Disease behavior (B2 vs. B1) | 1.18 | 0.49 | 2.83 | 0.71 |
|  (B3 vs. B1) | 0.73 | 0.32 | 1.68 | 0.45 |
| Use of IM (Yes vs No) | 0.94 | 0.58 | 1.52 | 0.79 |
| Smoke (Yes vs. No) | 0.61 | 0.35 | 1.05 | 0.07 |

The result indicates that there is a significant difference on the risk of having surgery between patients taken anti-TNF and no anti-TNF (hazard ratio, 3.57; 95% confidence interval [CI], 1.98 to 6.44; P-value <0.0001). Those treated with anti-TNF had a higher risk of having surgery comparing with patients with no anti-TNF therapy.

Crude Hazard ratio (without adjustment) = 2.44 (95% CI of 1.47 to 4.05).