**Supplementary Table 1:** Baseline characteristics, prophylactic measures and bleeding event managements in the TC and GSEED-RE2 score subgroups.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total cohort** |  | **Low DB riskδ** | **Medium DB riskδ**  | **High DB riskδ** |  | ***p*-Value** |
| **Patient characteristics; n(%)** | 2130(100%) |  | 1183(55.6%) | 690(32.4%) | 256(12.0%) |  |  |
| Male | 1301(62.3%) |  | 657 (57.0%) | 461 (67.6%) | 183 (72.0%) |  | <0.001\*\*\* |
| aAge | 68.2(10.6) |  | 65.7 (10.6) | 70.4 (9.9) | 74.4 (8.8) |  | <0.001\*\*\* |
| ASA III-IV or comorbidity | 1239 (58.2%) |  | 388 (32.8%) | 596 (86.4%) | 254 (99.2%) |  | <0.001\*\*\* |
| Antiplatelet/Anticoagulant | 544 (25.5%) |  | 16 (1.4%) | 271 (39.3%) | 256 (100%) |  | <0.001\*\*\* |
| **Polyp characteristics; n(%)** | 2263 (100%) |  | 1257(55.6%) | 738 (32.6%) | 267 (11.8%) |  |  |
| bSize (mm) | 30.8 (11.9) |  | 30.2 (11.9) | 32.5 (12.5) | 28.9 (10.0) |  | <0.001\*\*\* |
|  ≥40mm | 551 (24.4%) |  | 259 (20.6%) | 237 (32.2%) | 55 (20.6%) |  | 0.046\* |
| cProximal location | 1056(46.7%) |  | 329 (26.2%) | 460 (62.3%) | 267 (100%) |  | <0.001\*\*\* |
| Complete resection | 2002(90.1%) |  | 1128(91.6%) | 634 (87.6%) | 240 (90.2%) |  | 0.064 |
| **Clip closure; n(%)** | 525 (23.2%) |  | 271 (21.6%) | 177 (24.0%) | 77 (28.8%) |  | 0.010\* |
| **Delayed bleeding (DB); n(%)** | 93 (4.1%) |  | 31 (2.5%) | 28 (3.8%) | 34 (12.7%) |  | <0.001\*\*\* |
| * No clip closure
 | 78 (4.5%) |  | 28 (2.8%) | 24 (4.3%) | 26 (13.7%) |  | <0.001\*\*\* |
| * Clip closure
 | 15 (2.9%) |  | 3 (1.1%) | 4 (2.3%) | 8 (10.4%) |  | <0.001\*\*\* |
| **Bleeding treatment; n(%)** | 149 (6.6%) |  | 68 (5.4%) | 53 (7.2%) | 27 (10.1%) |  | 0.004\*\* |
| * Inyection
 | 11 (0.5%) |  | 4 (0.3%) | 5 (0.7%) | 2 (0.7%) |  |  |
| * Coagulation forceps
 | 13 (0.6%) |  | 6 (0.5%) | 7 (0.9%) | 0 (0.0%) |  |  |
| * ArgonPC
 | 18 (0.8%) |  | 5 (0.4%) | 11 (1.5%) | 2 (0.7%) |  |  |
| * Clipping
 | 55 (2.4%) |  | 29 (2.3%) | 13 (1.8%) | 13 (4.9%) |  |  |
| * ArgonPC+Clipping
 | 52 (2.3%) |  | 24 (1.9%) | 17 (2.3%) | 10 (3.7%) |  |  |
| * Embolization
 | 1 (0.044%) |  | 0 (0.0%) | 0 (0.0%) | 1 (0.4%) |  |  |
| Transfusion | 34 (1.5%) |  | 8 (0.6%) | 8 (1.1%) | 18 (6.7%) |  | <0.001\*\*\* |
| Surgery by bleeding | 0 (0%) |  | 0 (0%) | 0 (0%) | 0 (0%) |  |  |
| Hospitalization by bleeding | 84 (3.8%) |  | 28 (2.2%) | 28 (3.8%) | 27 (10.1%) |  | <0.001\*\*\* |

a Described as Mean (SD). b Described as Median (IQR). c Location from cecum to the hepatic flexure (included). **δ** GSEED-RE2 risk subgroup: low DB risk=’0-3 points’; medium DB risk= ‘4-6 points’; high risk=’7-9 points. \* Significant (p < 0.05), \*\* Very significant (p< 0.01) and \*\*\*Extremely significant (p < 0.001). Anova and Chi-squared Test used for comparisons

**Supplementary Table 2:** Costs associated with the management of DB in the TC and by DB risk subgroup.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Cost** **per unit** |  | **Total cohort** |  |  | **Low DB risk**δ | **Medium DB risk**δ | **High DB risk**δ |
| **DB management,** n(%) |  |  |  |  |  |  |  |
| Urgency attendance | 618.2€ |  | 93(100%) |  |  | 31(100%) | 28(100%) | 34(100%) |
| Colonoscopy + sedation | 785.3€ |  | 70(75.3%) |  |  | 23(74.2%) | 21(75.0%) | 26(76.5%) |
| Bleeding treatment | 367.3€ |  | 44(47.3%) |  |  | 11(41.9%) | 12(42.9%) | 19(55.9%) |
| Transfusion | 375.3€ |  | 29(31.2%) |  |  | 6 (19.4%) | 5 (17.9%) | 18(52.9%) |
| Days of hospitalization | 663.2€/day |  | 253 |  |  | 73 | 69 | 111 |
| **Total DB management cost** |  |  | 307,085€ |  |  | 92,858€ | 85,841€ | 128,386€ |
| **Average DB cost per DB event** |  | **3302.0€** |  |  | **2995.4€** | **3065.8€** | **3776.1€** |

*δ GSEED-RE2 risk subgroup: low DB risk=0-3 points; medium DB risk= 4-6 points; high risk=7-9 points.*

**Supplementary Table 3:** Comparison of different studies evaluating clip closure efficacy in LNPCPs >20 mm.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **N Polyps** | **Average size**  | **Clip interval** | **DB rate** | **DB risk relative reduction (RR)** |
| Albeniz, 2019$ | 235 | 36.0mm | 6mm | 12.1% (control) | 58.7% (Clip Closure) |
|   |   |   |   |   | 89.6% (Complete clip Closure) |
| Pohl, 2019 | 919 | 30.0mm | 7mm | 7.5% (control) | 50.7% (clip closure) |
|   |   |   |   | 9.6% (proximal polyps) | 65.6% (clip closure of proximal polyps) |

$ *Patients with an average-high risk of delayed bleeding by GSEED-RE score.*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Bahin, 2016** | **Parikh, 2013** | **Shah, 2019**  | **Albéniz et al.** |
| **N Polyps** | 1717 | No real data | 899 | 2263 |
| **Mean size:** | 35.8mm (E) | 12.5mm (A) | - | 30mm (E) |
| **DB risk (global)** | 6.4% (E) | 0.64% (A) | 7.0% € | 4.5% (E) |
| **DB risk subgroups** |   | Antiplatelets = 2.5% (A) Anticoagulant =3.4% (A)  |   | LowRisk=2.8% (E) |
| Proximal = 8.9% (E) | Proximal =9.5% (E) | MediumRisk=4.3% (E) |
|   |   | HighRisk (HR)=13.7% (E) |
| **DB risk relative reduction (RR)** | 75% (A) | 82% (A) | 70.7% (E) | Global=51.0% (E) |
| 100% (A) | (Proximal polyps) | HR=58.7% (E) |
| **Clip interval** | 3mm1(E) | 12.5mm (A) | - | 6mm (E) |
| **Clip price** | 81 € | 155$ | - | SP: 60 €US: 150 $  |
| **Prophylaxis cost** | 1.106 € | 165.54$ | 0$ | SP : 300 €US: 750 $ |
|  |  |  |  | SP: Global=3302.0€ (E) |
| **DB cost** | 2445€ (E) | 9150$ (A) | 6,458$ (E) | SP: HR=3776.1€ (E) |
|  |  |  |  | US: Global = 6500 $ (A) |
|  |  |  |  | US: HR= 7500 $ (A) |
| **Utility reduction by DB** | - | 1 day (A) | - | 0.0208 QALYs (A) |
| **Threshold for CE** | FNS=4500€ | ICER= 100000$/QALY |   | SP : ICER=54,000€/QALY |
| - | or |
|   | US: ICER=100,000$/QALY |
| **Threshold for CS** | - | - | - | ICER=0€/QALY |
| **Result for global clipping** | No cost-effective | No cost-effective | -  | No cost-effective |
| **Result for subgroup clipping** | No cost-effective | **Cost-effective**  | **Cost-saving** | **Cost-saving** (SP)**Cost-effective** (SP and US) |
| (Antiplatelets and anticoagulant) | (Proximal polyps) | (High-Risk) |
| **Minimum DB risk for universal CE** | - | 2.07% | - | 13.3% (SP)17.1% (US) |
| **Maximum clip price for universal CE** | 10.35€ | ~20$ | - | 20.3€ (SP)39.4$ (US) |

**Supplementary Table 4:** Comparison of different studies evaluating clip prophylaxis-related costs.

1 The number of clips were calculated by taking the size of the polyp, adding 2.5mm to each side, and then dividing it by the interval in mm. CE: Cost-effectiveness; CS: Cost-Saving; (A) Assumed; (E) Estimated from real data. HR: High-risk subcohort. SP: Spain. US: United States.