**Appendix Tables**

Table S1. Characteristics of included studies for cancer risk after splenectomy

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study (year) | Country | Study period | N (SP +/SP-) | Female (SP +/SP-) | Age (SP +/SP-) | Reason for SP | Follow-up period | Control | NOS score |
| Mellemkjoer et al, (1995a) | Danish | 1977-1989 | 1103/NA | 332/NA | 31/NA | Trauma | 6.8 years | General population | 7 |
| Mellemkjoer et al, (1995b) | Danish | 1977-1989 | 900/NA | 458/NA | NA /NA | Benign hematologic disorders | NA | General population | 7 |
| Linet et al, (1996a) | Swedish | 1965-1983 | 1295/NA | 396/NA | 29/NA | Trauma | 11.8 years | General population | 7 |
| Linet et al, (1996b) | Swedish | 1965-1983 | 985/NA | 415/NA | 56/NA | Non-malignant conditions of adjacent organs | 9.6 years | General population | 7 |
| Kristinsson et al, (2014) | America | 1969-1996 | 8149/ NA | 0/0 | NA/NA | Trauma | 27 years | Veterans | 8 |
| Sun et al, (2015a) | China | 2000-2006 | 2295/ 19592 | 662/7440 | 42/45 | Trauma | 7.41 years | General population | 6 |
| Sun et al, (2015b) | China | 2000-2006 | 2603/ 19592 | 1198/7440 | 48/45 | Nontrauma | 7.41 years | General population | 6 |
| Lv et al, (2016) | China | 2002-2012 | 359/ 2319 | 104/564 | 49/50 | Hypersplenism | NA | Hepatitis cirrhosis | 7 |
| Thai et al, (2016) | France | 1990-2004 | 83/ 83 | 60/69 | NA/NA | Immune thrombocytopenia | 192 months | Immune thrombocytopenia | 7 |
| Zhang et al, (2018) | China | 2008-2012 | 407/464 | NA/NA | NA/NA | Hypersplenism | 63 months | Hepatitis cirrhosis | 7 |

SP = splenectomy, NOS = Newcastle-Ottawa Scale, NA = data not available.

Table S2.Characteristics of included studies for splenectomy in gastric cancer

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study (year) | Country | Study period | Study design | N (SP +/SP-) | Female (SP +/SP-) | Age (SP +/SP-) | Pancreatectomy | Gastrectomy | Stage | Outcomes | NOS score |
| Kishimoto et al, (1979) | Japan | 1960-1971 | nRCT | 58/55 | NA/NA | NA/NA | mixed | Partial/total/proximal | I-IV | 5-year OS | 7 |
| Sugimachi et al, (1980) | Japan | 1964-1976 | nRCT | 47/30 | NA/NA | NA/NA | NA | Total | NA | 5-year OS | 7 |
| Miwa et al, (1983) | Japan | 1965-1981 | nRCT | 86/52 | NA/NA | NA/NA | NA | Total | III-IV | 5-year OS, complication | 7 |
| Suehiro et al, (1984) | Japan | 1970-1980 | nRCT | 53/50 | 18/25 | 57/54 | mixed | Total | I-IV | 5-year OS, mortality, complication | 7 |
| Lersch et al, (1985) | Germany | NA | nRCT | 64/38 | 20/16 | 63/62 | NA | NA | I-IV | complication, mortality | 6 |
| Brady et al, (1991) | America | 1960-1984 | nRCT | 163/229 | NA/NA | NA/NA | mixed | Distal/ proximal/ total/ esophagogastrectomy | NA | complication, mortality | 6 |
| Griffith et al, (1995) | United Kingdom | 1970-1989 | nRCT | 76/119 | 23/48 | 68/68 | mixed | Total/subtotal | I-III | 5-year OS, complication, mortality | 6 |
| Bonenkamp et al, (1995) | Netherlands | 1989-1993 | RCT | 165/542 | NA/NA | NA/NA | mixed | Distal/ total | NA | complication, mortality | NA |
| Cuschieri et al, (1996) | United Kingdom | NA | RCT | 193/207 | NA/NA | NA/NA | mixed | Distal/ total | NA | complication, mortality | NA |
| Otsuji et al, (1996) | Japan | 1983-1993 | nRCT | 154/91 | 60/30 | 58/63 | mixed | Total | I-IV | 5-year OS, complication | 7 |
| Kodera et al, (1997) | Japan | 1978-1993 | nRCT | 167/57 | NA/NA | NA/NA | mixed | Proximal/ total | I-IV | 5-year OS, complication, mortality | 7 |
| Kwon et al, (1997) | Korea | 1989-1993 | nRCT | 260/232 | 93/88 | NA/NA | NA | NA | I-IV | complication, mortality | 6 |
| Wanebo et al, (1997) | America | 1982-1987 | nRCT | 908/2555 | NA/NA | NA/NA | NA | Proximal/total/ distal/middle | I-IV | 5-year OS, mortality | 6 |
| Saji et al, (1999) | Japan | 1985-1987 | nRCT | 78/175 | 28/38 | 59/59 | mixed | Partial/total/proximal | I-IV | 5-year OS, complication, mortality | 7 |
| Otsuji et al, (1999) | Japan | 1983-1994 | nRCT | 103/25 | 40/7 | NA/66 | mixed | Total | I-IV | 5-year OS, complication | 8 |
| Kasakura et al, (2000) | Japan | 1980-1997 | nRCT | 183/1755 | 69/493 | NA/59 | mixed | Partial/total | I-IV | complication, mortality | 6 |
| Lee et al, (2001) | Korea | 1987-1996 | nRCT | 492/173 | 166/56 | 52/54 | NO | Total | I-IV | 5-year OS, mortality | 6 |
| Takeuchi et al, (2001) | Japan | 1985-1999 | nRCT | 65/98 | 18/27 | 63/66 | Yes | Total | I-IV | 5-year OS, complication, mortality | 6 |
| Lo et al, (2002) | China | 1987-1999 | nRCT | 87/201 | NA/27 | 64/68 | Yes | Total | I-IV | complication, mortality | 6 |
| Csendes et al, (2002) | Chile | 1985-1992 | RCT | 90/97 | NA/NA | NA/NA | NO | Total | NA | 5-year OS, complication, mortality | NA |
| Qin et al, (2002) | China | 1985-1998 | nRCT | 246/63 | 39/8 | NA/54.5 | mixed | NA | I-IV | 5-year OS, complication, mortality | 6 |
| Erturk et al, (2003) | Turkey | 1989-1993 | nRCT | 38/23 | 16/11 | 57/59 | NA | Proximal | I-IV | 5-year OS, complication | 8 |
| Kodera et al, (2005) | Japan | 1995-2001 | RCT | 191/332 | NA/NA | NA/NA | mixed | Distal/ proximal/ total | NA | complication | NA |
| Fatouros et al, (2005) | Greece | 1986-1992 | nRCT | 67/59 | 25/23 | 65/66 | mixed | Subtotal/ total | NA | complication, mortality | 7 |
| Gorbunov et al, (2005) | Czech Republic | 1990-1997 | nRCT | 40/243 | NA/NA | NA/NA | mixed | Distal/ proximal/ total | I-IV | 5-year OS | 6 |
| Toneri et al, (2006) | Japan | 1998-2005 | nRCT | 6/62 | NA/NA | NA/NA | NA | Distal/ total | NA | 5-year OS | 6 |
| Yu et al, (2006) | Korea | 1995-1999 | RCT | 104/103 | 72/72 | 57/57 | NO | Total | I-IV | 5-year OS, complication, mortality | NA |
| Zhang et al, (2007) | China | 1994-2003 | nRCT | 38/70 | 6/12 | 61/60 | mixed | Subtotal/ total | II-IV | 5-year OS, complication, mortality | 8 |
| Yonemura et al, (2008) | Japan | 1995-2005 | RCT | 124/145 | NA/NA | NA/NA | NA | Subtotal/ total/ proximal | II-IV | 5-year OS | NA |
| Sasada et al, (2009) | Japan | 1991-2006 | nRCT | 201/148 | 61/51 | 61/65 | mixed | Total | I-IV | 5-year OS, complication, mortality | 6 |
| Verlato et al, (2009) | Italy | 1988-2002 | nRCT | 141/891 | NA/NA | NA/NA | mixed | Subtotal/ total/ proximal | NA | 5-year OS, complication, mortality | 6 |
| Li et al, (2009) | Korea | 1991-2006 | nRCT | 62/69 | 21/19 | 53/53 | NA | Total | I-IV | 5-year OS, complication | 7 |
| Huang et al, (2009) | China | 1980-2002 | nRCT | 73/143 | 16/33 | NA/NA | NO | Proximal/ total | NA | 5-year OS, complication, mortality | 8 |
| Oh et al, (2009) | Korea | 2000-2004 | nRCT | 99/267 | 31/92 | NA/NA | NO | Total | I-III | 5-year OS, complication, mortality | 8 |
| Pacelli et al, (2011) | Italy | 1990-2005 | nRCT | 246/68 | NA /NA | NA/NA | mixed | Subtotal/ total | I-IV | 5-year OS | 6 |
| Yao et al, (2011) | China | NA | nRCT | 51/61 | 14/18 | 59/57 | NA | NA | I-IV | 5-year OS, complication, mortality | 9 |
| Nashimoto et al, (2012) | Japan | 1994-2004 | nRCT | 240/265 | 68/67 | NA/NA | NO | Total | II-IV | 5-year OS, complication | 7 |
| Wang et al, (2014) | China | 1994-2008 | nRCT | 172/291 | 51/65 | 65/65 | NA | Total | I-III | 5-year OS, complication, mortality | 8 |
| Zhang et al, (2014) | China | 1980-2003 | nRCT | 100/114 | 18/29 | 59/56 | NO | Subtotal/ total | I-IV | 5-year OS, complication | 7 |
| Ji et al, (2016a) | China | 2006-2011 | nRCT | 31/186 | 5/48 | NA/NA | NO | Proximal/ total | NA | 5-year OS, complication, mortality | 8 |
| Pan et al, (2016) | China | NA | nRCT | 49/57 | 18/21 | 58/59 | NA | Total | IV | complication | 6 |
| Ji et al, (2016b) | China | 2003-2010 | nRCT | 105/243 | 38/99 | 58/59 | NA | NA | NA | 5-year OS | 6 |
| Usui et al, (2016) | Japan | 2004-2014 | nRCT | 19/59 | 7 /10 | 62/65 | NO | Total | I-III | complication | 6 |
| Ohkura et al, (2017) | Japan | 1975-2015 | nRCT | 63/45 | 24/11 | 64/66 | NO | Subtotal/ total | I-III | 5-year OS, complication | 9 |
| Sano et al, (2017) | Japan | 2002-2009 | RCT | 254/251 | 58/47 | 654/65 | NO | Total | I-IV | 5-year OS, complication, mortality | NA |
| Son et al, (2017) | Korea | 2006-2012 | nRCT | 44/68 | 16/18 | 55/60 | NO | Total | I-III | 5-year OS, complication | 8 |
| Jeong et al, (2018) | Korea | 2006-2014 | nRCT | 97/97 | 28/30 | 62/62 | mixed | Total | I-IV | 5-year OS, complication, | 9 |
| Ding et al, (2019) | China | 1980-2012 | nRCT | 152/113 | 32/22 | NA/NA | mixed | Proximal/ total | II-III | 5-year OS, complication, mortality | 7 |
| Kinoshita et al, (2021) | Japan | 2012-2018 | nRCT | 63/82 | 29/21 | 64/67 | NO | Total | I-IV | 5-year OS, complication, mortality | 7 |
| Ito et al, (2021) | Japan | 2010-2014 | nRCT | 60/54 | 22/17 | 65/73 | NO | Total | I-III | 5-year OS, complication | 6 |

SP = splenectomy, NOS = Newcastle-Ottawa Scale, OS = overall survival, RCT = randomized controlled trials, nRCT = non-randomized controlled trials, NA = data not available, Stage = TNM Stages.

Table S3. The quality of the randomized controlled trials.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study (year) | Truly random | Concealed allocation | Baseline features | Eligibility criteria | Blinding assessment | Loss to follow-up | Intention to treat | Study quality |
| Bonenkamp et al, (1995) | Yes | Unclear | Unclear | Yes | Unclear | Yes | Unclear | Low |
| Cuschieri et al, (1996) | Yes | Unclear | Unclear | Yes | Unclear | Yes | Unclear | Low |
| Csendes et al, (2002) | Yes | Unclear | Yes | Yes | Unclear | Yes | No | Fair |
| Kodera et al, (2005) | Yes | Unclear | Unclear | Yes | Unclear | Yes | Unclear | Low |
| Yu et al, (2006) | Yes | Unclear | Yes | Yes | Unclear | Yes | Unclear | Fair |
| Yonemura et al, (2008) | Yes | Unclear | Unclear | Yes | Unclear | Yes | Unclear | Low |
| Sano et al, (2017) | Yes | Yes | Yes | Yes | Unclear | Yes | Yes | High |

Table S4. Characteristics of included studies for splenectomy in colorectal cancer

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study (year) | Country | Study period | N  (SP +/SP-) | Female  (SP +/SP-) | Age  (SP +/SP-) | Stage | Outcomes | NOS score |
| Davis et al, (1988) | Japan | 1966-1980 | 57/57 | 22/22 | NA/NA | B,C | 5-year OS, mortality | 7 |
| Varty et al, (1993) | United Kingdom | 1970-1988 | 21/21 | 10/10 | 69/65 | A,B,C,D | 5-year OS, complication, mortality | 8 |
| Konstadoulakis et al, (1999) | Greece | 1973-1990 | 25/25 | 11/11 | 68/64 | B,C | 5-year OS, complication | 8 |
| Wakeman et al, (2008) | New Zealand | 1990-1999 | 55/55 | 21/21 | 73/71 | NA | 5-year OS | 9 |

SP = splenectomy, NOS = Newcastle-Ottawa Scale, OS = overall survival, NA = data not available, Stage = Dukes’ Stage.

Table S5. Characteristics of included studies for splenectomy in esophageal cancer and esophago‑gastric junction cancer

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study (year) | Country | Study period | N  (SP +/SP-) | Female (SP +/SP-) | Age  (SP +/SP-) | Stage | Outcomes | NOS score |
| Kyriazanos et al, (2002) | Japan | 1981-1999 | 14/135 | NA/NA | 66/64 | 0-IV | complication, mortality | 8 |
| Gockel et al, (2005) | Germany | 1985-2003 | 34/370 | 8/62 | 58/56 | I-IV | 5-year OS, complication, mortality | 9 |
| Black et al, (2006) | United Kingdom | 1991-2004 | 48/690 | 19/185 | NA/NA | NA | complication, mortality | 7 |
| Pultrum et al, (2008) | Netherlands | 1991-2004 | 64/144 | 11/32 | 63/64 | I-IV | 5-year OS, complication, mortality | 6 |
| Aminian et al, (2010) | Iran | 2001-2006 | 14/406 | 6/195 | 66/63 | NA | complication, mortality | 8 |
| Fukuchi et al, (2018) | Japan | 2005-2017 | 20/40 | NA/NA | NA/NA | I-IV | 5-year OS | 6 |

SP = splenectomy, NOS = Newcastle-Ottawa Scale, OS = overall survival, NA = data not available, Stage = TNM Stages.

Table S6. Characteristics of included studies for splenectomy in liver cancer

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study (year) | Country | Study period | N (SP +/SP-) | Female (SP +/SP-) | Age (SP +/SP-) | Child-Pugh classification | Outcomes | NOS score |
| Nagasue et al, (1999) | Japan | 1988-1999 | 26/36 | 11/5 | NA/NA | B,C | 5-year OS, complication, mortality | 7 |
| Oh et al, (2003) | Korea | 1986-2003 | 12/6 | 3/2 | 49/59 | A,B | mortality | 6 |
| Wu et al, (2004) | China | 1989-2002 | 41/485 | 13/93 | 60/59 | A,B,C | complication, mortality | 7 |
| Chen et al, (2005) | China | 1993-2001 | 94/110 | 14/21 | 45/42 | A,B | 5-year OS, complication | 8 |
| Jiang et al, (2007) | China | 1997-2003 | 61/82 | 2/5 | 47/45 | A,B | 5-year OS, complication | 7 |
| Sugimachi et al, (2008) | Japan | 1989-2005 | 4/11 | NA/NA | NA/NA | A,B | complication, mortality | 6 |
| Kim et al, (2013) | Korea | 2000-2009 | 19/39 | 6/6 | 51/56 | A | 5-year OS, complication, mortality | 7 |
| Li et al, (2014) | China | 1999-2013 | 60/121 | 14/21 | 55/56 | A,B | complication, mortality | 8 |
| Zhang et al, (2015) | China | 1999-2013 | 84/84 | 15/15 | 49/51 | A | 5-year OS, complication | 8 |
| Yang et al, (2016) | China | 2001-2011 | 31/44 | 3/6 | 51/52 | A,B | 5-year OS, complication, mortality | 7 |
| Zhang et al, (2017) | China | 2007-2015 | 110/271 | 19/42 | 50/50 | NA | 5-year OS, complication, mortality | 7 |
| Takeishi et al, (2018) | Japan | 2004-2010 | 22/18 | 11/6 | 62/64 | A,B | 5-year OS, complication | 6 |
| Pei et al, (2019) | China | 2005-2015 | 95/95 | 13/14 | 52/52 | B | 5-year OS, complication | 8 |
| Zhou et al, (2021) | China | 2011-2016 | 103/122 | 26/20 | 51/52 | A,B | 5-year OS, complication, mortality | 7 |

SP = splenectomy, NOS = Newcastle-Ottawa Scale, OS = overall survival, NA = data not available.

Table S7. Subgroup meta-analyses of mortality after splenectomy for gastric cancer

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Subgroup | Studies, n | SP+, n | SP-, n | Risk Ratio (95% CI) | P Value | Heterogeneity χ2(P value) | Inconsistency I2(%) |
| RCT | 5 | 806 | 1200 | 3.575 (2.284, 5.596) | <0.001 | 6.94 (0.139) | 42.4% |
| nRCT | 21 | 3738 | 7747 | 1.224 (1.010, 1.482) | 0.039 | 21.08 (0.393) | 5.1% |
| Total gastrectomy | 11 | 1693 | 1709 | 0.906 (0.544, 1.508) | 0.703 | 6.33 (0.787) | 0% |
| Pancreasectomy | 6 | 446 | 2381 | 1.980 (1.165, 3.368) | 0.012 | 12.28 (0.031) | 59.3% |
| Nopancreasectomy | 11 | 1638 | 3311 | 2.015 (1.198, 3.388) | 0.008 | 5.24 (0.874) | 0% |

CI = confidence intervals.