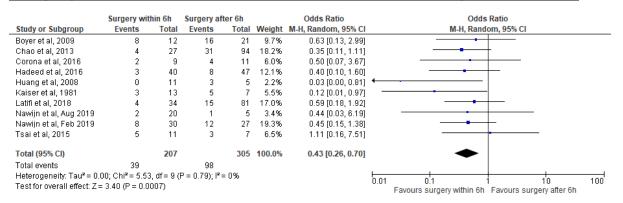
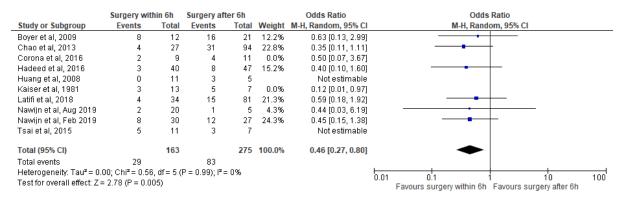
Additional file 4 Forrest plots for all (subgroup) analyses assessing surgical timing in relation to mortality and amputation due to necrotizing soft tissue infections

Surgery within 6 hours after presentation - mortality as outcome



Subgroup analysis: High-quality studies



Subgroup analysis: Studies published ≥2009

| | Surgery wit | hin 6h | Surgery af | ter 6h | | Odds Ratio | Odds Ratio |
|---------------------------------------|-----------------------------|-------------|---------------------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Boyer et al, 2009 | 8 | 12 | 16 | 21 | 10.5% | 0.63 [0.13, 2.99] | |
| Chao et al, 2013 | 4 | 27 | 31 | 94 | 19.7% | 0.35 [0.11, 1.11] | |
| Corona et al, 2016 | 2 | 9 | 4 | 11 | 6.5% | 0.50 [0.07, 3.67] | |
| Hadeed et al, 2016 | 3 | 40 | 8 | 47 | 13.1% | 0.40 [0.10, 1.60] | |
| Huang et al, 2008 | 0 | 11 | 3 | 5 | 0.0% | 0.03 [0.00, 0.81] | |
| Kaiser et al, 1981 | 3 | 13 | 5 | 7 | 0.0% | 0.12 [0.01, 0.97] | |
| Latifi et al, 2018 | 4 | 34 | 15 | 81 | 18.4% | 0.59 [0.18, 1.92] | |
| Nawijn et al, Aug 2019 | 2 | 20 | 1 | 5 | 3.7% | 0.44 [0.03, 6.19] | |
| Nawijn et al, Feb 2019 | 8 | 30 | 12 | 27 | 21.0% | 0.45 [0.15, 1.38] | |
| Tsai et al, 2015 | 5 | 11 | 3 | 7 | 7.1% | 1.11 [0.16, 7.51] | |
| Total (95% CI) | | 183 | | 293 | 100.0% | 0.49 [0.30, 0.82] | ◆ |
| Total events | 36 | | 90 | | | | |
| Heterogeneity: Tau ² = 0.0 | 00; Chi ² = 1.31 | , df = 7 (l | P = 0.99); I ² | = 0% | | | |
| Test for overall effect: Z = | 2.73 (P = 0.0 | 06) | | | | | 0.01 0.1 1 10 100 Favours surgery within 6h Favours surgery after 6h |
| | | | | | | | Favours surgery within on Favours surgery after on |

Subgroup analysis: Studies without limitation on affected body region by NSTI

| | Surgery wit | hin 6h | Surgery af | ter 6h | | Odds Ratio | Odds Ratio |
|---------------------------------------|-------------|------------|------------|--------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Boyer et al, 2009 | 8 | 12 | 16 | 21 | 0.0% | 0.63 [0.13, 2.99] | |
| Chao et al, 2013 | 4 | 27 | 31 | 94 | 22.1% | 0.35 [0.11, 1.11] | |
| Corona et al, 2016 | 2 | 9 | 4 | 11 | 0.0% | 0.50 [0.07, 3.67] | |
| Hadeed et al, 2016 | 3 | 40 | 8 | 47 | 14.8% | 0.40 [0.10, 1.60] | |
| Huang et al, 2008 | 0 | 11 | 3 | 5 | 0.0% | 0.03 [0.00, 0.81] | |
| Kaiser et al, 1981 | 3 | 13 | 5 | 7 | 6.7% | 0.12 [0.01, 0.97] | |
| Latifi et al, 2018 | 4 | 34 | 15 | 81 | 20.7% | 0.59 [0.18, 1.92] | |
| Nawijn et al, Aug 2019 | 2 | 20 | 1 | 5 | 4.2% | 0.44 [0.03, 6.19] | |
| Nawijn et al, Feb 2019 | 8 | 30 | 12 | 27 | 23.6% | 0.45 [0.15, 1.38] | |
| Tsai et al, 2015 | 5 | 11 | 3 | 7 | 8.0% | 1.11 [0.16, 7.51] | |
| Total (95% CI) | | 175 | | 268 | 100.0% | 0.44 [0.25, 0.75] | • |
| Total events | 29 | | 75 | | | | |
| Heterogeneity: Tau ² = 0.1 | | 3 df = 6 (| | = 0% | | | |
| Test for overall effect: Z = | | | 0.01/11 | | | | 0.01 0.1 1 10 100 |
| - correction of orall effect. Z - | | 007 | | | | | Favours surgery within 6h Favours surgery after 6h |

| | Surgery wit | hin 6h | Surgery af | ter 6h | | Odds Ratio | Odds Ratio |
|--------------------------------------|-----------------------------|-------------|---------------------------|--------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% CI |
| Boyer et al, 2009 | 8 | 12 | 16 | 21 | 13.3% | 0.63 [0.13, 2.99] | |
| Chao et al, 2013 | 4 | 27 | 31 | 94 | 0.0% | 0.35 [0.11, 1.11] | |
| Corona et al, 2016 | 2 | 9 | 4 | 11 | 8.2% | 0.50 [0.07, 3.67] | |
| Hadeed et al, 2016 | 3 | 40 | 8 | 47 | 16.6% | 0.40 [0.10, 1.60] | |
| Huang et al, 2008 | 0 | 11 | 3 | 5 | 0.0% | 0.03 [0.00, 0.81] | |
| Kaiser et al, 1981 | 3 | 13 | 5 | 7 | 7.5% | 0.12 [0.01, 0.97] | |
| Latifi et al, 2018 | 4 | 34 | 15 | 81 | 23.2% | 0.59 [0.18, 1.92] | |
| Nawijn et al, Aug 2019 | 2 | 20 | 1 | 5 | 4.7% | 0.44 [0.03, 6.19] | |
| Nawijn et al, Feb 2019 | 8 | 30 | 12 | 27 | 26.5% | 0.45 [0.15, 1.38] | |
| Tsai et al, 2015 | 5 | 11 | 3 | 7 | 0.0% | 1.11 [0.16, 7.51] | |
| Total (95% CI) | | 158 | | 199 | 100.0% | 0.45 [0.25, 0.79] | • |
| Total events | 30 | | 61 | | | | |
| Heterogeneity: Tau ² = 0. | 00; Chi ² = 1.95 | 5, df = 6 (| P = 0.92); I ² | = 0% | | | |
| Test for overall effect: Z = | • | | | | | | 0.01 0.1 1 10 100 |
| | | , | | | | | Favours surgery within 6h Favours surgery after 6h |

Surgery within 6 hours after presentation - amputation as outcome

| | Surgery wit | hin 6h | Surgery af | ter 6h | | Odds Ratio | Odds Ratio |
|--------------------------------------|-----------------------------|-------------|-----------------------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Corona et al, 2016 | 1 | 9 | 3 | 11 | 8.4% | 0.33 [0.03, 3.93] | |
| Hadeed et al, 2016 | 6 | 29 | 13 | 31 | 38.6% | 0.36 [0.11, 1.14] | |
| Huang et al, 2008 | 4 | 11 | 0 | 5 | 5.2% | 6.60 [0.29, 149.77] | |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 4.1% | 0.11 [0.00, 3.70] | · · · · · · · · · · · · · · · · · · · |
| Mittapalli et al, 2015 | 2 | 6 | 3 | 18 | 11.5% | 2.50 [0.31, 20.45] | |
| Nawijn et al, Aug 2019 | 1 | 14 | 0 | 4 | 4.5% | 1.00 [0.03, 29.19] | |
| Nawijn et al, Feb 2019 | 4 | 16 | 3 | 15 | 17.6% | 1.33 [0.24, 7.28] | |
| Tsai et al, 2015 | 2 | 11 | 2 | 7 | 10.1% | 0.56 [0.06, 5.24] | |
| Total (95% CI) | | 103 | | 94 | 100.0% | 0.68 [0.34, 1.39] | - |
| Total events | 20 | | 25 | | | | |
| Heterogeneity: Tau ² = 0. | 00; Chi ² = 6.72 | 2, df = 7 (| P = 0.46); I ² : | = 0% | | | |
| Test for overall effect: Z = | = 1.05 (P = 0.3 | 0) | | | | | 0.01 0.1 1 10 100 Favours surgery within 6h Favours surgery after 6h |

Subgroup analysis: High-quality studies

| | Surgery wit | thin 6h | Surgery af | ter 6h | | Odds Ratio | Odds Ratio |
|--------------------------------------|-----------------------------|-------------|-----------------------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% CI |
| Corona et al, 2016 | 1 | 9 | 3 | 11 | 0.0% | 0.33 [0.03, 3.93] | |
| Hadeed et al, 2016 | 6 | 29 | 13 | 31 | 63.6% | 0.36 [0.11, 1.14] | |
| Huang et al, 2008 | 4 | 11 | 0 | 5 | | Not estimable | |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 0.0% | 0.11 [0.00, 3.70] | |
| Mittapalli et al, 2015 | 2 | 6 | 3 | 18 | 0.0% | 2.50 [0.31, 20.45] | |
| Nawijn et al, Aug 2019 | 1 | 14 | 0 | 4 | 7.4% | 1.00 [0.03, 29.19] | |
| Nawijn et al, Feb 2019 | 4 | 16 | 3 | 15 | 29.1% | 1.33 [0.24, 7.28] | |
| Tsai et al, 2015 | 2 | 11 | 2 | 7 | | Not estimable | |
| Total (95% CI) | | 59 | | 50 | 100.0% | 0.57 [0.23, 1.42] | |
| Total events | 11 | | 16 | | | | |
| Heterogeneity: Tau ² = 0. | 00; Chi ² = 1.68 | 3, df = 2 (| P = 0.43); I ² = | = 0% | | | |
| Test for overall effect: Z | | | | | | | 0.01 0.1 1 10 100 Favours surgery within 6h Favours surgery after 6h |

Subgroup analysis: Studies published ≥2009

| | Surgery wit | hin 6h | Surgery aff | ter 6h | | Odds Ratio | Odds Ratio |
|---------------------------------------|-----------------------------|------------|-----------------------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Corona et al, 2016 | 1 | 9 | 3 | 11 | 9.2% | 0.33 [0.03, 3.93] | |
| Hadeed et al, 2016 | 6 | 29 | 13 | 31 | 42.6% | 0.36 [0.11, 1.14] | |
| Huang et al, 2008 | 4 | 11 | 0 | 5 | 0.0% | 6.60 [0.29, 149.77] | |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 0.0% | 0.11 [0.00, 3.70] | |
| Mittapalli et al, 2015 | 2 | 6 | 3 | 18 | 12.7% | 2.50 [0.31, 20.45] | |
| Nawijn et al, Aug 2019 | 1 | 14 | 0 | 4 | 4.9% | 1.00 [0.03, 29.19] | |
| Nawijn et al, Feb 2019 | 4 | 16 | 3 | 15 | 19.5% | 1.33 [0.24, 7.28] | |
| Tsai et al, 2015 | 2 | 11 | 2 | 7 | 11.1% | 0.56 [0.06, 5.24] | |
| Total (95% CI) | | 85 | | 86 | 100.0% | 0.65 [0.31, 1.38] | - |
| Total events | 16 | | 24 | | | | |
| Heterogeneity: Tau ² = 0.1 | 00; Chi ² = 3.64 | , df = 5 (| P = 0.60); I ² = | = 0% | | | |
| Test for overall effect: Z = | = 1.12 (P = 0.2 | 6) | | | | | 0.01 0.1 1 10 100 Favours surgery within 6h Favours surgery after 6h |

Subgroup analysis: Studies without limitation on affected body region by NSTI

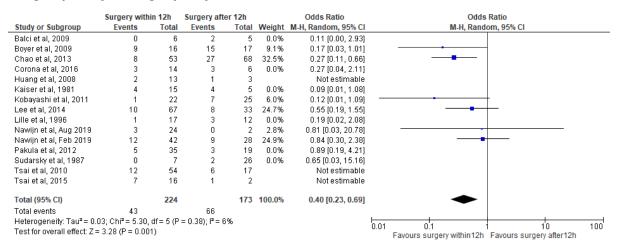
| Huang et al, 2008 4 11 0 5 0.0% 6.60 [0.29, 149.77] Kaiser et al, 1981 0 7 1 3 4.8% 0.11 [0.00, 3.70] Mittapalli et al, 2015 2 6 3 18 13.3% 2.50 [0.31, 20.45] Nawijn et al, Aug 2019 1 14 0 4 5.2% 1.00 [0.03, 29.19] Nawijn et al, Feb 2019 4 16 3 15 20.4% 1.33 [0.24, 7.28] Tsai et al, 2015 2 11 2 7 11.7% 0.56 [0.06, 5.24] Total events 15 22 22 15 22 Heterogeneity: Tau ² = 0.00: Chi ² = 4.33; df = 5 (P = 0.50): P = 0% 0% 0.64 [0.30, 1.38] | | n Odds Ratio Odds Ratio | Sur | |
|--|--------------------------|--|---------|----|
| Hadeed et al, 2016 6 29 13 31 44.7% 0.36 [0.11, 1.14] Huang et al, 2008 4 11 0 5 0.0% 6.60 [0.29, 149.77] Kaiser et al, 1981 0 7 1 3 4.8% 0.11 [0.00, 3.70] Wittapalli et al, 2015 2 6 3 18 13.3% 2.50 [0.31, 20.45] Nawijn et al, Feb 2019 1 14 0 4 5.2% 1.00 [0.03, 29.19] Nawijn et al, Feb 2019 4 16 3 15 20.4% 1.33 [0.24, 7.28] Total (95% Cl) 83 78 100.0% 0.64 [0.30, 1.38] Total events 15 22 22 15 22 Heterogenetic Tau ² = 0.00°, Ch ² = 4 33. off = 5 (P = 0.50°, P = 0.5%) 15 16 16 | tudy or Subgroup | tal Weight M-H, Random, 95% Cl M-H, Random, 95% Cl | I Ev | |
| Huang et al, 2008 4 11 0 5 0.0% 6.60 [0.29, 149.77] Kaiser et al, 1981 0 7 1 3 4.8% 0.11 [0.00, 3.70] Mittapalli et al, 2015 2 6 3 18 13.3% 2.50 [0.31, 20.45] Nawijn et al, Aug 2019 1 14 0 4 5.2% 1.00 [0.03, 29.19] Nawijn et al, Feb 2019 4 16 3 15 20.4% 1.33 [0.24, 7.28] Tsai et al, 2015 2 11 2 7 11.7% 0.56 [0.06, 5.24] Total events 15 22 22 15 22 Heterogeneity: Tau ² = 0.00: Ch ² = 4.33; df = 5 (P = 0.50); P = 0% 0% 0.64 [0.30, 1.38] | orona et al, 2016 | 11 0.0% 0.33 [0.03, 3.93] |) | |
| Kaiser et al, 1981 0 7 1 3 4.8% 0.11 [0.00, 3.70] Mittapalli et al, 2015 2 6 3 18 13.3% 2.50 [0.31, 20.45] Nawijn et al, Aug 2019 1 14 0 4 5.2% 1.00 [0.03, 29.19] Nawijn et al, Feb 2019 4 16 3 15 20.4% 1.33 [0.24, 7.28] Tsai et al, 2015 2 11 2 7 11.7% 0.56 [0.06, 5.24] Total (95% CI) 83 78 100.0% 0.64 [0.30, 1.38] Total events 15 22 Heterogenetik: Tauž= 0.00: Chiz = 4 33 df = 5 (P = 0.50): (P = 0% | ladeed et al, 2016 | 31 44.7% 0.36 [0.11, 1.14] |) | |
| Mittapalli et al, 2015 2 6 3 18 13.3% 2.50 [0.31, 20.45] Nawijn et al, Aug 2019 1 14 0 4 5.2% 1.00 [0.03, 29.19] Nawijn et al, Feb 2019 4 16 3 15 20.4% 1.33 [0.24, 7.28] Tsai et al, 2015 2 11 2 7 11.7% 0.56 [0.06, 5.24] Total (95% Cl) 83 78 100.0% 0.64 [0.30, 1.38] Total events 15 22 22 Heterogenepits Tauj= -0.00; Chiz= -0.30; If = 5 (P = 0.50); IE = 0.0% 14 14 14 | luang et al, 2008 | 5 0.0% 6.60 [0.29, 149.77] | | |
| Nawijn et al, Aug 2019 1 14 0 4 5.2% 1.00 [0.03, 29.19] Nawijn et al, Feb 2019 4 16 3 15 20.4% 1.33 [0.24, 7.28] Tsai et al, 2015 2 11 2 7 11.7% 0.56 [0.06, 5.24] Total (95% CI) 83 78 100.0% 0.64 [0.30, 1.38] Total events 15 22 Heterogenetic Tau2 = 0.00: Chi² = 4.33 df = 5 (P = 0.50); P = 0.0% | aiser et al, 1981 | 3 4.8% 0.11 [0.00, 3.70] | , | |
| Nawijn et al, Feb 2019 4 16 3 15 20.4% 1.33 [0.24, 7.28] Tsai et al, 2015 2 11 2 7 11.7% 0.56 [0.06, 5.24] Total (95% CI) 83 78 100.0% 0.64 [0.30, 1.38] Total events 15 22 Heterogeneity: Tau ² = 0.00: Chi ² = 4.33 df = 5 (P = 0.50): I ² = 0% | littapalli et al, 2015 | 18 13.3% 2.50 [0.31, 20.45] |) | |
| Tsai et al, 2015 2 11 2 7 11.7% 0.58 [0.06, 5.24] Total (95% Cl) 83 78 100.0% 0.64 [0.30, 1.38] Total events 15 22 Heterogenetity Tau2 = 0.00: Cbi2 = 4.33 df = 5 (P = 0.50): P = 0% | lawijn et al, Aug 2019 | 4 5.2% 1.00 [0.03, 29.19] | Ļ | - |
| Total (95% CI) 83 78 100.0% 0.64 [0.30, 1.38] | lawijn et al, Feb 2019 | 15 20.4% 1.33 [0.24, 7.28] | 6 | |
| Total events 15 22 Heterographic Tau? = 0.00: Chi? = 4.33 df = 5 (P = 0.50): P = 0% | sai et al, 2015 | 7 11.7% 0.56 [0.06, 5.24] | | |
| Heterogeneity: Tau2 = 0.00; Cbi2 = 4.33, df = 5 (P = 0.50); I2 = 0% | otal (95% CI) | 78 100.0% 0.64 [0.30, 1.38] | 3 | |
| Heterogeneity: Tau ² = 0.00; Chi ² = 4.33, df = 5 (P = 0.50); I ² = 0% | otal events | | | |
| | leterogeneity: Tau² = 0. | | (P = 0) | |
| | | 0.01 0.1 1 10 Favours surgerv within 6h Favours surgerv after 6 | · - | 10 |

| | Surgery wit | hin 6h | Surgery af | ter 6h | | Odds Ratio | Odds Ratio |
|---------------------------------------|-----------------------------|------------|-----------------------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Corona et al, 2016 | 1 | 9 | 3 | 11 | 9.9% | 0.33 [0.03, 3.93] | |
| Hadeed et al, 2016 | 6 | 29 | 13 | 31 | 45.6% | 0.36 [0.11, 1.14] | |
| Huang et al, 2008 | 4 | 11 | 0 | 5 | 0.0% | 6.60 [0.29, 149.77] | |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 4.9% | 0.11 [0.00, 3.70] | · · · · · · · · · · · · · · · · · · · |
| Mittapalli et al, 2015 | 2 | 6 | 3 | 18 | 13.6% | 2.50 [0.31, 20.45] | |
| Nawijn et al, Aug 2019 | 1 | 14 | 0 | 4 | 5.3% | 1.00 [0.03, 29.19] | |
| Nawijn et al, Feb 2019 | 4 | 16 | 3 | 15 | 20.8% | 1.33 [0.24, 7.28] | |
| Tsai et al, 2015 | 2 | 11 | 2 | 7 | 0.0% | 0.56 [0.06, 5.24] | |
| Total (95% CI) | | 81 | | 82 | 100.0% | 0.61 [0.28, 1.32] | |
| Total events | 14 | | 23 | | | | |
| Heterogeneity: Tau ² = 0.0 | 00; Chi ² = 4.57 | , df = 5 (| P = 0.47); I ² : | = 0% | | | |
| Test for overall effect: Z = | | | | | | | 0.01 0.1 1 10 100 Favours surgery within 6h Favours surgery after 6h |
| | | | | | | | avours surgery within on Favours surgery alter on |

Surgery within 12 hours after presentation - mortality as outcome

| | Surgery with | in 12h | Surgery after | er 12h | | Odds Ratio | Odds Ratio |
|--------------------------------------|-------------------------------|-----------|-----------------------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Balci et al, 2009 | 0 | 6 | 2 | 5 | 1.6% | 0.11 [0.00, 2.93] | · · · · · · · · · · · · · · · · · · · |
| Boyer et al, 2009 | 9 | 16 | 15 | 17 | 5.4% | 0.17 [0.03, 1.01] | |
| Chao et al, 2013 | 8 | 53 | 27 | 68 | 21.3% | 0.27 [0.11, 0.66] | |
| Corona et al, 2016 | 3 | 14 | 3 | 6 | 4.1% | 0.27 [0.04, 2.11] | |
| Huang et al, 2008 | 2 | 13 | 1 | 3 | 2.1% | 0.36 [0.02, 6.19] | |
| Kaiser et al, 1981 | 4 | 15 | 4 | 5 | 2.8% | 0.09 [0.01, 1.08] | · |
| Kobayashi et al, 2011 | 1 | 22 | 7 | 25 | 3.6% | 0.12 [0.01, 1.09] | |
| Lee et al, 2014 | 10 | 67 | 8 | 33 | 15.7% | 0.55 [0.19, 1.55] | |
| Lille et al, 1996 | 1 | 17 | 3 | 12 | 3.0% | 0.19 [0.02, 2.08] | |
| Nawijn et al, Aug 2019 | 3 | 24 | 0 | 2 | 1.6% | 0.81 [0.03, 20.78] | |
| Nawijn et al, Feb 2019 | 12 | 42 | 9 | 28 | 15.9% | 0.84 [0.30, 2.38] | |
| Pakula et al, 2012 | 5 | 35 | 3 | 19 | 7.1% | 0.89 [0.19, 4.21] | |
| Sudarsky et al, 1987 | 0 | 7 | 2 | 26 | 1.7% | 0.65 [0.03, 15.16] | |
| Tsai et al, 2010 | 12 | 54 | 6 | 17 | 12.2% | 0.52 [0.16, 1.71] | |
| Tsai et al, 2015 | 7 | 16 | 1 | 2 | 2.0% | 0.78 [0.04, 14.75] | |
| Total (95% CI) | | 401 | | 268 | 100.0% | 0.41 [0.27, 0.61] | ◆ |
| Total events | 77 | | 91 | | | | |
| Heterogeneity: Tau ² = 0. | .00; Chi ² = 9.31, | df = 14 (| P = 0.81); I ² = | 0% | | | |
| Test for overall effect: Z: | = 4.27 (P < 0.00 | 01) | | | | | 0.01 0.1 i 10 100 Favours surgery within 12h Favours surgery after 12h |

Subgroup analysis: High-quality studies



Subgroup analysis: Studies published ≥2009

| | Surgery with | in 12h | Surgery after | er 12h | | Odds Ratio | Odds Ratio |
|---------------------------------------|------------------|------------|-----------------------------|--------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Balci et al, 2009 | 0 | 6 | 2 | 5 | 1.7% | 0.11 [0.00, 2.93] | · • · · · · · · · · · · · · · · · · · · |
| Boyer et al, 2009 | 9 | 16 | 15 | 17 | 6.0% | 0.17 [0.03, 1.01] | |
| Chao et al, 2013 | 8 | 53 | 27 | 68 | 23.6% | 0.27 [0.11, 0.66] | _ |
| Corona et al, 2016 | 3 | 14 | 3 | 6 | 4.5% | 0.27 [0.04, 2.11] | · · · · · · · · · · · · · · · · · · · |
| Huang et al, 2008 | 2 | 13 | 1 | 3 | 0.0% | 0.36 [0.02, 6.19] | |
| Kaiser et al, 1981 | 4 | 15 | 4 | 5 | 0.0% | 0.09 [0.01, 1.08] | |
| Kobayashi et al, 2011 | 1 | 22 | 7 | 25 | 3.9% | 0.12 [0.01, 1.09] | · |
| Lee et al, 2014 | 10 | 67 | 8 | 33 | 17.4% | 0.55 [0.19, 1.55] | _ |
| Lille et al, 1996 | 1 | 17 | 3 | 12 | 0.0% | 0.19 [0.02, 2.08] | |
| Nawijn et al, Aug 2019 | 3 | 24 | 0 | 2 | 1.8% | 0.81 [0.03, 20.78] | |
| Nawijn et al, Feb 2019 | 12 | 42 | 9 | 28 | 17.5% | 0.84 [0.30, 2.38] | |
| Pakula et al, 2012 | 5 | 35 | 3 | 19 | 7.8% | 0.89 [0.19, 4.21] | |
| Sudarsky et al, 1987 | 0 | 7 | 2 | 26 | 0.0% | 0.65 [0.03, 15.16] | |
| Tsai et al, 2010 | 12 | 54 | 6 | 17 | 13.5% | 0.52 [0.16, 1.71] | |
| Tsai et al, 2015 | 7 | 16 | 1 | 2 | 2.2% | 0.78 [0.04, 14.75] | · · · · · · · · · · · · · · · · · · · |
| Total (95% CI) | | 349 | | 222 | 100.0% | 0.43 [0.28, 0.67] | ◆ |
| Total events | 70 | | 81 | | | | |
| Heterogeneity: Tau ² = 0.0 | 00; Chi² = 7.32, | df = 10 (l | P = 0.69); I ² = | 0% | | | 0.01 0.1 1 10 100 |
| Test for overall effect: Z = | 3.76 (P = 0.00 | 02) | | | | | Favours surgery within 12h Favours surgery after 12h |

Subgroup analysis: Studies without limitation on affected body region by NSTI

| | Surgery within | n 12h | Surgery afte | r 12 h | | Odds Ratio | Odds Ratio |
|--------------------------------------|--------------------|------------|--|---------------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% Cl |
| Balci et al, 2009 | 0 | 6 | 2 | 5 | 0.0% | 0.11 [0.00, 2.93] | |
| Boyer et al, 2009 | 9 | 16 | 15 | 17 | 0.0% | 0.17 [0.03, 1.01] | |
| Chao et al, 2013 | 8 | 53 | 27 | 68 | 24.5% | 0.27 [0.11, 0.66] | |
| Corona et al, 2016 | 3 | 14 | 3 | 6 | 0.0% | 0.27 [0.04, 2.11] | |
| Huang et al, 2008 | 2 | 13 | 1 | 3 | 0.0% | 0.36 [0.02, 6.19] | |
| Kaiser et al, 1981 | 4 | 15 | 4 | 5 | 3.2% | 0.09 [0.01, 1.08] | • • • |
| Kobayashi et al, 2011 | 1 | 22 | 7 | 25 | 4.1% | 0.12 [0.01, 1.09] | |
| Lee et al, 2014 | 10 | 67 | 8 | 33 | 18.1% | 0.55 [0.19, 1.55] | |
| Lille et al, 1996 | 1 | 17 | 3 | 12 | 3.4% | 0.19 [0.02, 2.08] | |
| Nawijn et al, Aug 2019 | 3 | 24 | 0 | 2 | 1.9% | 0.81 [0.03, 20.78] | |
| Nawijn et al, Feb 2019 | 12 | 42 | 9 | 28 | 18.3% | 0.84 [0.30, 2.38] | |
| Pakula et al, 2012 | 5 | 35 | 3 | 19 | 8.1% | 0.89 [0.19, 4.21] | |
| Sudarsky et al, 1987 | 0 | 7 | 2 | 26 | 2.0% | 0.65 [0.03, 15.16] | · · · · · · · · · · · · · · · · · · · |
| Tsai et al, 2010 | 12 | 54 | 6 | 17 | 14.0% | 0.52 [0.16, 1.71] | |
| Tsai et al, 2015 | 7 | 16 | 1 | 2 | 2.3% | 0.78 [0.04, 14.75] | |
| Total (95% CI) | | 352 | | 237 | 100.0% | 0.45 [0.29, 0.70] | ◆ |
| Total events | 63 | | 70 | | | | |
| Heterogeneity: Tau ² = 0. | 00; Chi² = 7.44, d | df = 10 (l | ^o = 0.68); I ^z = 0 | 1% | | | |
| Test for overall effect: Z = | = 3.54 (P = 0.000 | 14) | | | | | 0.01 0.1 1 1 10 100 Favours surgery within 12h Favours surgery after 12h |

| | Surgery with | in 12h | Surgery afte | r 12h | | Odds Ratio | Odds Ratio |
|--------------------------------------|------------------------------|-----------|-------------------------------------|-------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Balci et al, 2009 | 0 | 6 | 2 | 5 | 3.4% | 0.11 [0.00, 2.93] | ← → − − − |
| Boyer et al, 2009 | 9 | 16 | 15 | 17 | 11.6% | 0.17 [0.03, 1.01] | |
| Chao et al, 2013 | 8 | 53 | 27 | 68 | 0.0% | 0.27 [0.11, 0.66] | |
| Corona et al, 2016 | 3 | 14 | 3 | 6 | 8.7% | 0.27 [0.04, 2.11] | |
| Huang et al, 2008 | 2 | 13 | 1 | 3 | 0.0% | 0.36 [0.02, 6.19] | |
| Kaiser et al, 1981 | 4 | 15 | 4 | 5 | 6.0% | 0.09 [0.01, 1.08] | · · · · · · · · · · · · · · · · · · · |
| Kobayashi et al, 2011 | 1 | 22 | 7 | 25 | 7.6% | 0.12 [0.01, 1.09] | |
| Lee et al, 2014 | 10 | 67 | 8 | 33 | 0.0% | 0.55 [0.19, 1.55] | |
| Lille et al, 1996 | 1 | 17 | 3 | 12 | 6.3% | 0.19 [0.02, 2.08] | |
| Nawijn et al, Aug 2019 | 3 | 24 | 0 | 2 | 3.5% | 0.81 [0.03, 20.78] | |
| Nawijn et al, Feb 2019 | 12 | 42 | 9 | 28 | 34.0% | 0.84 [0.30, 2.38] | |
| Pakula et al, 2012 | 5 | 35 | 3 | 19 | 15.1% | 0.89 [0.19, 4.21] | |
| Sudarsky et al, 1987 | 0 | 7 | 2 | 26 | 3.7% | 0.65 [0.03, 15.16] | |
| Tsai et al, 2010 | 12 | 54 | 6 | 17 | 0.0% | 0.52 [0.16, 1.71] | |
| Tsai et al, 2015 | 7 | 16 | 1 | 2 | 0.0% | 0.78 [0.04, 14.75] | |
| Total (95% CI) | | 198 | | 145 | 100.0% | 0.41 [0.22, 0.74] | ◆ |
| Total events | 38 | | 48 | | | | |
| Heterogeneity: Tau ² = 0. | 00; Chi ² = 7.83, | df = 9 (P | = 0.55); I ² = 09 | % | | | |
| Test for overall effect: Z : | = 2.92 (P = 0.00 | 3) | | | | | 0.01 0.1 1 10 100 Favours surgery within 12h Favours surgery after 12h |

Surgery within 12 hours after presentation - amputation as outcome

| | Surgery with | in 12h | Surgery afte | r 12h | | Odds Ratio | Odds Ratio | |
|---------------------------------------|------------------------------|-----------|------------------------------|-------|--------|---------------------|---|-----|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl | |
| Corona et al, 2016 | 2 | 14 | 2 | 6 | 17.3% | 0.33 [0.03, 3.20] | | |
| Huang et al, 2008 | 4 | 13 | 0 | 3 | 8.8% | 3.32 [0.14, 78.81] | | _ |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 7.2% | 0.11 [0.00, 3.70] | • • • | |
| Mittapalli et al, 2015 | 2 | 8 | 3 | 16 | 21.4% | 1.44 [0.19, 11.04] | | |
| Nawijn et al, Aug 2019 | 1 | 17 | 0 | 1 | 6.8% | 0.27 [0.01, 10.09] | • • • | |
| Nawijn et al, Feb 2019 | 4 | 21 | 3 | 11 | 30.0% | 0.63 [0.11, 3.49] | | |
| Tsai et al, 2015 | 4 | 16 | 0 | 2 | 8.5% | 1.80 [0.07, 45.14] | | |
| Total (95% CI) | | 96 | | 42 | 100.0% | 0.71 [0.28, 1.82] | | |
| Total events | 17 | | 9 | | | | | |
| Heterogeneity: Tau ² = 0.1 | 00; Chi ² = 3.51, | df = 6 (P | = 0.74); l ² = 09 | % | | | | |
| Test for overall effect: Z = | = 0.71 (P = 0.48 |) | | | | | 0.01 0.1 1 10 Favours surgery within 12h Favours surgery after 12h | 100 |

Subgroup analysis: High-quality studies

| | Surgery with | in 12h | Surgery after | 12h | | Odds Ratio | Odds Ratio |
|---------------------------------------|------------------------------|-----------|------------------------------|-------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% Cl |
| Corona et al, 2016 | 2 | 14 | 2 | 6 | 0.0% | 0.33 [0.03, 3.20] | |
| Huang et al, 2008 | 4 | 13 | 0 | 3 | | Not estimable | |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 0.0% | 0.11 [0.00, 3.70] | |
| Mittapalli et al, 2015 | 2 | 8 | 3 | 16 | 0.0% | 1.44 [0.19, 11.04] | |
| Nawijn et al, Aug 2019 | 1 | 17 | 0 | 1 | 18.4% | 0.27 [0.01, 10.09] | • |
| Nawijn et al, Feb 2019 | 4 | 21 | 3 | 11 | 81.6% | 0.63 [0.11, 3.49] | |
| Tsai et al, 2015 | 4 | 16 | 0 | 2 | | Not estimable | |
| Total (95% CI) | | 38 | | 12 | 100.0% | 0.54 [0.11, 2.54] | |
| Total events | 5 | | 3 | | | | |
| Heterogeneity: Tau ² = 0.1 | 00; Chi ² = 0.17, | df = 1 (P | = 0.68); I ² = 09 | 6 | | | |
| Test for overall effect: Z = | = 0.78 (P = 0.43) |) | | | | | 0.01 0.1 1 10 100 Favours surgery within 12h Favours surgery after 12h |

Subgroup analysis: Studies published ≥2009

| | Surgery with | in 12h | Surgery afte | r 12h | | Odds Ratio | | Odds Ratio | |
|--------------------------------------|------------------|-----------|--|-------|--------|---------------------|------|---|-----|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | | M-H, Random, 95% Cl | |
| Corona et al, 2016 | 2 | 14 | 2 | 6 | 20.6% | 0.33 [0.03, 3.20] | | | |
| Huang et al, 2008 | 4 | 13 | 0 | 3 | 0.0% | 3.32 [0.14, 78.81] | | | |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 0.0% | 0.11 [0.00, 3.70] | | | |
| Mittapalli et al, 2015 | 2 | 8 | 3 | 16 | 25.5% | 1.44 [0.19, 11.04] | | | |
| Nawijn et al, Aug 2019 | 1 | 17 | 0 | 1 | 8.1% | 0.27 [0.01, 10.09] | • | | |
| Nawijn et al, Feb 2019 | 4 | 21 | 3 | 11 | 35.7% | 0.63 [0.11, 3.49] | | | |
| Tsai et al, 2015 | 4 | 16 | 0 | 2 | 10.1% | 1.80 [0.07, 45.14] | | | - |
| Total (95% CI) | | 76 | | 36 | 100.0% | 0.71 [0.25, 1.98] | | | |
| Total events | 13 | | 8 | | | | | | |
| Heterogeneity: Tau ² = 0. | 00; Chi² = 1.51, | df = 4 (P | = 0.82); I ^z = 0 ^o | % | | | L | | 400 |
| Test for overall effect: Z | = 0.66 (P = 0.51 |) | | | | | 0.01 | 0.1 1 10 Favours surgery within12h Favours surgery after 12h | 100 |

Subgroup analysis: Studies without limitation on affected body region by NSTI

| | Surgery with | in 12h | Surgery after | r 12h | | Odds Ratio | Odds Ratio |
|---|--------------|--------|------------------------------|-------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% CI |
| Corona et al, 2016 | 2 | 14 | 2 | 6 | 0.0% | 0.33 [0.03, 3.20] | |
| Huang et al, 2008 | 4 | 13 | 0 | 3 | 0.0% | 3.32 [0.14, 78.81] | |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 9.7% | 0.11 [0.00, 3.70] | ← |
| Mittapalli et al, 2015 | 2 | 8 | 3 | 16 | 28.9% | 1.44 [0.19, 11.04] | |
| Nawijn et al, Aug 2019 | 1 | 17 | 0 | 1 | 9.2% | 0.27 [0.01, 10.09] | • • • |
| Nawijn et al, Feb 2019 | 4 | 21 | 3 | 11 | 40.6% | 0.63 [0.11, 3.49] | |
| Tsai et al, 2015 | 4 | 16 | 0 | 2 | 11.5% | 1.80 [0.07, 45.14] | |
| Total (95% CI) | | 69 | | 33 | 100.0% | 0.71 [0.24, 2.11] | |
| Total events | 11 | | 7 | | | | |
| Heterogeneity: Tau ² = 0.1 Test for overall effect: Z = | | | = 0.71); I ^z = 09 | 6 | | | 0.01 0.1 10 10 Favours surgery within 12h Favours surgery after 12h |

| | Surgery withi | n 12h | Surgery after | 12h | | Odds Ratio | Odds Ratio |
|---------------------------------------|--------------------|-----------|------------------------------|-------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% CI |
| Corona et al, 2016 | 2 | 14 | 2 | 6 | 20.9% | 0.33 [0.03, 3.20] | |
| Huang et al, 2008 | 4 | 13 | 0 | 3 | 0.0% | 3.32 [0.14, 78.81] | |
| Kaiser et al, 1981 | 0 | 7 | 1 | 3 | 8.7% | 0.11 [0.00, 3.70] | · · · · · · · · · · · · · · · · · · · |
| Mittapalli et al, 2015 | 2 | 8 | 3 | 16 | 25.9% | 1.44 [0.19, 11.04] | |
| Nawijn et al, Aug 2019 | 1 | 17 | 0 | 1 | 8.2% | 0.27 [0.01, 10.09] | · · · · · · |
| Nawijn et al, Feb 2019 | 4 | 21 | 3 | 11 | 36.3% | 0.63 [0.11, 3.49] | |
| Tsai et al, 2015 | 4 | 16 | 0 | 2 | 0.0% | 1.80 [0.07, 45.14] | |
| Total (95% CI) | | 67 | | 37 | 100.0% | 0.55 [0.19, 1.54] | |
| Total events | 9 | | 9 | | | | |
| Heterogeneity: Tau ² = 0.1 | 00; Chi² = 2.02, (| df = 4 (P | = 0.73); I ² = 0% | 6 | | | |
| Test for overall effect: Z = | = 1.14 (P = 0.25) | | | | | | 0.01 0.1 1 10 100 Favours surgery within 12h Favours surgery after 12h |

Surgery within 24 hours after presentation - mortality as outcome

| | Surgery with | in 24h | Surgery aft | er 24h | | Odds Ratio | | Odds Ratio |
|---------------------------------------|------------------------------|-----------|----------------|--------|--------|---------------------|------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | | M-H, Random, 95% Cl |
| Bair et al, 2009 | 8 | 38 | 10 | 68 | 10.3% | 1.55 [0.55, 4.33] | | |
| Balci et al, 2009 | 1 | 8 | 1 | 3 | 1.6% | 0.29 [0.01, 6.91] | | |
| Boyer et al, 2009 | 23 | 32 | 1 | 1 | 1.5% | 0.82 [0.03, 22.09] | | |
| Chao et al, 2013 | 20 | 90 | 15 | 31 | 12.7% | 0.30 [0.13, 0.72] | | |
| Corona et al, 2016 | 6 | 18 | 0 | 2 | 1.6% | 2.60 [0.11, 62.57] | | |
| George et al, 2009 | 8 | 61 | 0 | 11 | 1.9% | 3.65 [0.20, 67.92] | | |
| Huang et al, 2008 | 2 | 14 | 1 | 2 | 1.6% | 0.17 [0.01, 3.89] | ← | |
| Huang et al, 2011 | 38 | 280 | 19 | 192 | 18.1% | 1.43 [0.80, 2.56] | | + |
| Kaiser et al, 1981 | 6 | 17 | 2 | 3 | 2.3% | 0.27 [0.02, 3.67] | | |
| Kalaivani et al, 2012 | 10 | 35 | 5 | 25 | 8.2% | 1.60 [0.47, 5.44] | | |
| Lee et al, 2014 | 12 | 81 | 6 | 19 | 9.0% | 0.38 [0.12, 1.18] | | |
| Nawijn et al, Feb 2019 | 14 | 51 | 7 | 20 | 9.4% | 0.70 [0.23, 2.12] | | |
| Ogilvie et al, 2006 | 13 | 134 | 1 | 16 | 3.4% | 1.61 [0.20, 13.21] | | |
| Palmer et al, 1995 | 10 | 21 | 3 | 9 | 5.3% | 1.82 [0.36, 9.27] | | |
| Park et al, 2016 | 4 | 20 | 3 | 10 | 4.7% | 0.58 [0.10, 3.33] | | |
| Stephenson et al, 1992 | 2 | 7 | 12 | 22 | 4.3% | 0.33 [0.05, 2.10] | | |
| Wang et al, 1992 | 3 | 14 | 3 | 4 | 2.3% | 0.09 [0.01, 1.22] | • | |
| Yu et al, 2004 | 2 | 10 | 0 | 3 | 1.5% | 2.06 [0.08, 54.80] | | |
| Total (95% CI) | | 931 | | 441 | 100.0% | 0.79 [0.52, 1.20] | | • |
| Total events | 182 | | 89 | | | | | |
| Heterogeneity: Tau ² = 0.1 | 6; Chi ² = 22.03, | df = 17 (| P = 0.18); P = | 23% | | | | 0.1 1 10 100 |
| Test for overall effect: Z = | | | | | | | 0.01 | 0.1 1 10 100 Favours surgery within24h Favours surgery after 24h |

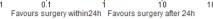
Subgroup analysis: High-quality studies

| | Surgery with | in 24h | Surgery aft | er 24h | | Odds Ratio | Odds Ratio |
|---------------------------------------|-----------------------------|-----------|---------------------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Bair et al, 2009 | 8 | 38 | 10 | 68 | 0.0% | 1.55 [0.55, 4.33] | |
| Balci et al, 2009 | 1 | 8 | 1 | 3 | 0.0% | 0.29 [0.01, 6.91] | |
| Boyer et al, 2009 | 23 | 32 | 1 | 1 | 4.7% | 0.82 [0.03, 22.09] | |
| Chao et al, 2013 | 20 | 90 | 15 | 31 | 24.8% | 0.30 [0.13, 0.72] | |
| Corona et al, 2016 | 6 | 18 | 0 | 2 | 0.0% | 2.60 [0.11, 62.57] | |
| George et al, 2009 | 8 | 61 | 0 | 11 | 0.0% | 3.65 [0.20, 67.92] | |
| Huang et al, 2008 | 2 | 14 | 1 | 2 | 0.0% | 0.17 [0.01, 3.89] | |
| Huang et al, 2011 | 38 | 280 | 19 | 192 | 30.0% | 1.43 [0.80, 2.56] | |
| Kaiser et al, 1981 | 6 | 17 | 2 | 3 | 0.0% | 0.27 [0.02, 3.67] | |
| Kalaivani et al, 2012 | 10 | 35 | 5 | 25 | 0.0% | 1.60 [0.47, 5.44] | |
| Lee et al, 2014 | 12 | 81 | 6 | 19 | 19.9% | 0.38 [0.12, 1.18] | |
| Nawijn et al, Feb 2019 | 14 | 51 | 7 | 20 | 20.6% | 0.70 [0.23, 2.12] | |
| Ogilvie et al, 2006 | 13 | 134 | 1 | 16 | 0.0% | 1.61 [0.20, 13.21] | |
| Palmer et al, 1995 | 10 | 21 | 3 | 9 | 0.0% | 1.82 [0.36, 9.27] | |
| Park et al, 2016 | 4 | 20 | 3 | 10 | 0.0% | 0.58 [0.10, 3.33] | |
| Stephenson et al, 1992 | 2 | 7 | 12 | 22 | 0.0% | 0.33 [0.05, 2.10] | |
| Wang et al, 1992 | 3 | 14 | 3 | 4 | 0.0% | 0.09 [0.01, 1.22] | |
| Yu et al, 2004 | 2 | 10 | 0 | 3 | 0.0% | 2.06 [0.08, 54.80] | |
| Total (95% CI) | | 534 | | 263 | 100.0% | 0.63 [0.29, 1.34] | - |
| Total events | 107 | | 48 | | | | |
| Heterogeneity: Tau ² = 0.4 | 1; Chi ² = 10.30 | df = 4 (P | = 0.04); l ² = | 61% | | | |
| Test for overall effect: Z = | 1.20 (P = 0.23) | | | | | | 0.01 0.1 1 10 10 Favours surgery within24h Favours surgery after 24h |

Subgroup analysis: Studies published ≥2009

| | | in 24h | | ter 24h | | Odds Ratio | Odds Ratio |
|------------------------|--------|--------|--------|---------|--------|---------------------|---------------------------------------|
| tudy or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% CI |
| air et al, 2009 | 8 | 38 | 10 | 68 | 6.9% | 1.55 [0.55, 4.33] | |
| alci et al, 2009 | 1 | 8 | 1 | 3 | 0.9% | 0.29 [0.01, 6.91] | · · · · · · · · · · · · · · · · · · · |
| oyer et al, 2009 | 23 | 32 | 1 | 1 | 0.8% | 0.82 [0.03, 22.09] | |
| hao et al, 2013 | 20 | 90 | 15 | 31 | 9.0% | 0.30 [0.13, 0.72] | |
| orona et al, 2016 | 6 | 18 | 0 | 2 | 0.9% | 2.60 [0.11, 62.57] | |
| eorge et al, 2009 | 8 | 61 | 0 | 11 | 1.1% | 3.65 [0.20, 67.92] | |
| iolena et al, 2011 | 471 | 4755 | 458 | 5203 | 30.4% | 1.14 [1.00, 1.30] | - |
| luang et al, 2008 | 2 | 14 | 1 | 2 | 0.0% | 0.17 [0.01, 3.89] | |
| luang et al, 2011 | 38 | 280 | 19 | 192 | 14.8% | 1.43 [0.80, 2.56] | |
| aiser et al, 1981 | 6 | 17 | 2 | 3 | 0.0% | 0.27 [0.02, 3.67] | |
| alaivani et al, 2012 | 10 | 35 | 5 | 25 | 5.2% | 1.60 [0.47, 5.44] | |
| ee et al, 2014 | 12 | 81 | 6 | 19 | 5.8% | 0.38 [0.12, 1.18] | |
| lawijn et al, Feb 2019 | 14 | 51 | 7 | 20 | 6.1% | 0.70 [0.23, 2.12] | |
| gilvie et al, 2006 | 13 | 134 | 1 | 16 | 0.0% | 1.61 [0.20, 13.21] | |
| almer et al, 1995 | 10 | 21 | 3 | 9 | 0.0% | 1.82 [0.36, 9.27] | |
| ark et al, 2016 | 4 | 20 | 3 | 10 | 2.8% | 0.58 [0.10, 3.33] | |
| tephenson et al, 1992 | 2 | 7 | 12 | 22 | 0.0% | 0.33 [0.05, 2.10] | |
| ugihara et al, 2012 | 42 | 262 | 23 | 117 | 15.4% | 0.78 [0.44, 1.37] | |
| Vang et al, 1992 | 3 | 14 | 3 | 4 | 0.0% | 0.09 [0.01, 1.22] | |
| u et al, 2004 | 2 | 10 | 0 | 3 | 0.0% | 2.06 [0.08, 54.80] | |
| otal (95% CI) | | 5731 | | 5702 | 100.0% | 0.92 [0.68, 1.25] | • |
| otal events | 657 | | 548 | | | | |

Test for overall effect: Z = 0.53 (P = 0.60)



Subgroup analysis: Studies without limitation on affected body region by NSTI

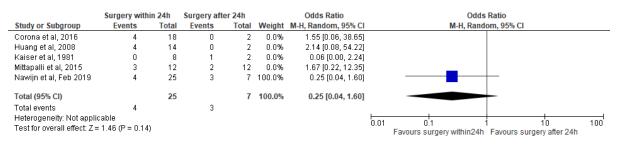
| | Surgery with | in 24h | Surgery aft | er 24h | | Odds Ratio | | Odds Ratio |
|---------------------------------------|-------------------------------|-----------|-----------------------------|--------|--------|---------------------|------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | | M-H, Random, 95% Cl |
| Bair et al, 2009 | 8 | 38 | 10 | 68 | 12.7% | 1.55 [0.55, 4.33] | | |
| Balci et al, 2009 | 1 | 8 | 1 | 3 | 0.0% | 0.29 [0.01, 6.91] | | |
| Boyer et al, 2009 | 23 | 32 | 1 | 1 | 0.0% | 0.82 [0.03, 22.09] | | |
| Chao et al, 2013 | 20 | 90 | 15 | 31 | 15.3% | 0.30 [0.13, 0.72] | | |
| Corona et al, 2016 | 6 | 18 | 0 | 2 | 0.0% | 2.60 [0.11, 62.57] | | |
| George et al, 2009 | 8 | 61 | 0 | 11 | 2.5% | 3.65 [0.20, 67.92] | | |
| Huang et al, 2008 | 2 | 14 | 1 | 2 | 0.0% | 0.17 [0.01, 3.89] | | |
| Huang et al, 2011 | 38 | 280 | 19 | 192 | 20.8% | 1.43 [0.80, 2.56] | | + |
| Kaiser et al, 1981 | 6 | 17 | 2 | 3 | 3.1% | 0.27 [0.02, 3.67] | | |
| Kalaivani et al, 2012 | 10 | 35 | 5 | 25 | 10.2% | 1.60 [0.47, 5.44] | | |
| Lee et al, 2014 | 12 | 81 | 6 | 19 | 11.1% | 0.38 [0.12, 1.18] | | - |
| Nawijn et al, Feb 2019 | 14 | 51 | 7 | 20 | 11.6% | 0.70 [0.23, 2.12] | | |
| Ogilvie et al, 2006 | 13 | 134 | 1 | 16 | 4.5% | 1.61 [0.20, 13.21] | | |
| Palmer et al, 1995 | 10 | 21 | 3 | 9 | 0.0% | 1.82 [0.36, 9.27] | | |
| Park et al, 2016 | 4 | 20 | 3 | 10 | 6.1% | 0.58 [0.10, 3.33] | | |
| Stephenson et al, 1992 | 2 | 7 | 12 | 22 | 0.0% | 0.33 [0.05, 2.10] | | |
| Wang et al, 1992 | 3 | 14 | 3 | 4 | 0.0% | 0.09 [0.01, 1.22] | | |
| Yu et al, 2004 | 2 | 10 | 0 | 3 | 2.0% | 2.06 [0.08, 54.80] | | |
| Total (95% CI) | | 817 | | 398 | 100.0% | 0.85 [0.53, 1.38] | | ◆ |
| Total events | 135 | | 68 | | | | | |
| Heterogeneity: Tau ² = 0.2 | 20; Chi ² = 15.31, | df = 10 (| P = 0.12); I ² = | 35% | | | 0.01 | 0.1 1 10 100 |
| Test for overall effect: Z = | | | | | | | 0.01 | 0.1 1 10 100 Favours surgery within24h Favours surgery after 24h |
| | | | | | | | | Favours surgery within2411 Favours surgery alter 2411 |

| | Surgery with | in 24h | Surgery aft | er 24h | | Odds Ratio | Odds Ratio |
|---------------------------------------|--------------|----------|----------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Bair et al, 2009 | 8 | 38 | 10 | 68 | 12.6% | 1.55 [0.55, 4.33] | |
| Balci et al, 2009 | 1 | 8 | 1 | 3 | 1.3% | 0.29 [0.01, 6.91] | · · · · · · · · · · · · · · · · · · · |
| Boyer et al, 2009 | 23 | 32 | 1 | 1 | 1.2% | 0.82 [0.03, 22.09] | |
| Chao et al, 2013 | 20 | 90 | 15 | 31 | 0.0% | 0.30 [0.13, 0.72] | |
| Corona et al, 2016 | 6 | 18 | 0 | 2 | 1.3% | 2.60 [0.11, 62.57] | |
| George et al, 2009 | 8 | 61 | 0 | 11 | 1.6% | 3.65 [0.20, 67.92] | · · · · · · · · · · · · · · · · · · · |
| Huang et al, 2008 | 2 | 14 | 1 | 2 | 1.3% | 0.17 [0.01, 3.89] | · |
| Huang et al, 2011 | 38 | 280 | 19 | 192 | 39.1% | 1.43 [0.80, 2.56] | - + |
| Kaiser et al, 1981 | 6 | 17 | 2 | 3 | 2.0% | 0.27 [0.02, 3.67] | |
| Kalaivani et al, 2012 | 10 | 35 | 5 | 25 | 8.9% | 1.60 [0.47, 5.44] | |
| Lee et al, 2014 | 12 | 81 | 6 | 19 | 0.0% | 0.38 [0.12, 1.18] | |
| Nawijn et al, Feb 2019 | 14 | 51 | 7 | 20 | 10.9% | 0.70 [0.23, 2.12] | |
| Ogilvie et al, 2006 | 13 | 134 | 1 | 16 | 3.0% | 1.61 [0.20, 13.21] | |
| Palmer et al, 1995 | 10 | 21 | 3 | 9 | 5.0% | 1.82 [0.36, 9.27] | |
| Park et al, 2016 | 4 | 20 | 3 | 10 | 4.4% | 0.58 [0.10, 3.33] | |
| Stephenson et al, 1992 | 2 | 7 | 12 | 22 | 3.9% | 0.33 [0.05, 2.10] | |
| Wang et al, 1992 | 3 | 14 | 3 | 4 | 2.0% | 0.09 [0.01, 1.22] | · · · · · · · · · · · · · · · · · · · |
| Yu et al, 2004 | 2 | 10 | 0 | 3 | 1.2% | 2.06 [0.08, 54.80] | |
| Total (95% CI) | | 760 | | 391 | 100.0% | 1.11 [0.77, 1.60] | * |
| Total events | 150 | | 68 | | | | |
| Heterogeneity: Tau ² = 0.0 | | df= 15 (| P = 0.63); P = | 0% | | | |
| Test for overall effect: Z = | | | | | | | 0.01 0.1 1 10 10 |
| | | | | | | | Favours surgery within24h Favours surgery after 24h |

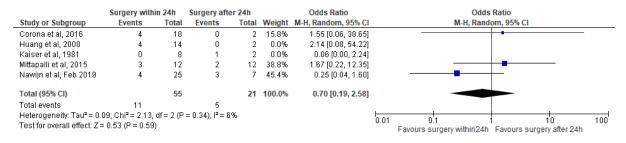
Surgery within 24 hours after presentation - amputation as outcome

| | Surgery with | in 24h | Surgery after | r 24h | | Odds Ratio | | Odds Ratio | |
|--------------------------------------|------------------------------|-----------|------------------------------|-------|--------|---------------------|------|---|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | | M-H, Random, 95% Cl | |
| Corona et al, 2016 | 4 | 18 | 0 | 2 | 12.6% | 1.55 [0.06, 38.65] | | | |
| Huang et al, 2008 | 4 | 14 | 0 | 2 | 12.5% | 2.14 [0.08, 54.22] | | | |
| Kaiser et al, 1981 | 0 | 8 | 1 | 2 | 10.0% | 0.06 [0.00, 2.24] | ← | | |
| Mittapalli et al, 2015 | 3 | 12 | 2 | 12 | 30.1% | 1.67 [0.22, 12.35] | | | - |
| Nawijn et al, Feb 2019 | 4 | 25 | 3 | 7 | 34.9% | 0.25 [0.04, 1.60] | | | |
| Total (95% CI) | | 77 | | 25 | 100.0% | 0.63 [0.20, 2.05] | | | |
| Total events | 15 | | 6 | | | | | | |
| Heterogeneity: Tau ² = 0. | 15; Chi ² = 4.34, | df = 4 (P | = 0.36); I ² = 89 | 6 | | | | | |
| Test for overall effect: Z | = 0.76 (P = 0.45 |) | | | | | 0.01 | 0.1 1 10 Favours surgery within24h Favours surgery a | |

Subgroup analysis: High-quality studies



Subgroup analysis: Studies published ≥2009

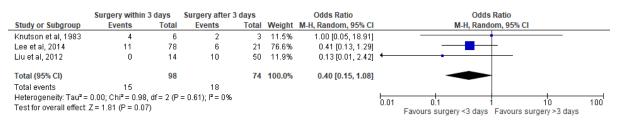


Subgroup analysis: Studies without limitation on affected body region by NSTI

| | Surgery with | in 24h | Surgery after | er 24h | | Odds Ratio | Odds Ratio |
|---------------------------------------|-----------------------------|-----------|-----------------------------|--------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | I M-H, Random, 95% CI |
| Corona et al, 2016 | 4 | 18 | 0 | 2 | 0.0% | 1.55 [0.06, 38.65] |] |
| Huang et al, 2008 | 4 | 14 | 0 | 2 | 0.0% | 2.14 [0.08, 54.22] | 1 |
| Kaiser et al, 1981 | 0 | 8 | 1 | 2 | 17.4% | 0.06 [0.00, 2.24] |] |
| Mittapalli et al, 2015 | 3 | 12 | 2 | 12 | 39.4% | 1.67 [0.22, 12.35] |] |
| Nawijn et al, Feb 2019 | 4 | 25 | 3 | 7 | 43.1% | 0.25 [0.04, 1.60] | |
| Total (95% CI) | | 45 | | 21 | 100.0% | 0.41 [0.08, 2.26] | |
| Total events | 7 | | 6 | | | | |
| Heterogeneity: Tau ² = 0.8 | 6; Chi ² = 3.22, | df = 2 (P | = 0.20); I ² = 3 | 8% | | | |
| Test for overall effect: Z = | 1.02 (P = 0.31) |) | | | | | 0.01 0.1 1 10 100 Favours surgery within24h Favours surgery after 24h |

| | Surgery with | in 24h | Surgery aft | er 24h | | Odds Ratio | | Odds | Ratio | |
|--|------------------|--------|-------------|--------|--------|---------------------|------|------------------------------------|---------------------------------|-----|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | | M-H, Rando | om, 95% Cl | |
| Corona et al, 2016 | 4 | 18 | 0 | 2 | 15.6% | 1.55 [0.06, 38.65] | | | • | |
| Huang et al, 2008 | 4 | 14 | 0 | 2 | 0.0% | 2.14 [0.08, 54.22] | | | | |
| Kaiser et al, 1981 | 0 | 8 | 1 | 2 | 12.5% | 0.06 [0.00, 2.24] | ← | | | |
| Mittapalli et al, 2015 | 3 | 12 | 2 | 12 | 33.7% | 1.67 [0.22, 12.35] | | | - | |
| Nawijn et al, Feb 2019 | 4 | 25 | 3 | 7 | 38.1% | 0.25 [0.04, 1.60] | | | _ | |
| Total (95% CI) | | 63 | | 23 | 100.0% | 0.53 [0.14, 2.06] | | | | |
| Total events | 11 | | 6 | | | | | | | |
| Heterogeneity: Tau ² = 0.38; Chi ² = 3.71, df = 3 (P = 0.29); l ² = 19% | | | | | | | | | | |
| Test for overall effect: Z | = 0.92 (P = 0.36 |) | | | | | 0.01 | 0.1 1 Favours surgery within24h | 10 Favours surgery after 24h | 100 |

Surgery within 3 days after onset symptoms - mortality as outcome



Subgroup analysis: High-quality studies

| | Surgery within | 3 days | Surgery after | 3 days | | Odds Ratio | Odds Ratio |
|--------------------------|--------------------|--------|---------------|--------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% Cl |
| Knutson et al, 1983 | 4 | 6 | 2 | 3 | | Not estimable | |
| Lee et al, 2014 | 11 | 78 | 6 | 21 | 100.0% | 0.41 [0.13, 1.29] | |
| Liu et al, 2012 | 0 | 14 | 10 | 50 | 0.0% | 0.13 [0.01, 2.42] | |
| Total (95% CI) | | 78 | | 21 | 100.0% | 0.41 [0.13, 1.29] | |
| Total events | 11 | | 6 | | | | |
| Heterogeneity: Not ap | plicable | | | | | F | |
| Test for overall effect: | Z = 1.53 (P = 0.13 |) | | | | U | 0.01 0.1 1 10 100 Favours surgery <3 days Favours surgery >3 days |

Subgroup analysis: Studies published ≥2009

| | Surgery within | 3 days | Surgery after 3 | days | | Odds Ratio | Odds Ratio |
|-----------------------------------|--------------------------------|-----------|------------------------------|-------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Knutson et al, 1983 | 4 | 6 | 2 | 3 | 0.0% | 1.00 [0.05, 18.91] | |
| Lee et al, 2014 | 11 | 78 | 6 | 21 | 86.6% | 0.41 [0.13, 1.29] | |
| Liu et al, 2012 | 0 | 14 | 10 | 50 | 13.4% | 0.13 [0.01, 2.42] | · |
| Total (95% CI) | | 92 | | 71 | 100.0% | 0.35 [0.12, 1.02] | |
| Total events | 11 | | 16 | | | | |
| Heterogeneity: Tau ² = | 0.00; Chi ² = 0.56, | df = 1 (P | = 0.45); I ² = 0% | | | | |
| Test for overall effect: | Z = 1.92 (P = 0.05 |) | | | | | 0.01 0.1 1 10 100 Favours surgery <3 days Favours surgery >3 days |

Subgroup analysis: Studies without limitation on affected body region by NSTI

| | Surgery within | 3 days | Surgery after 3 | days | | Odds Ratio | Odds Ratio |
|---|----------------|--------|-----------------|-------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | CI M-H, Random, 95% CI |
| Knutson et al, 1983 | 4 | 6 | 2 | 3 | 13.1% | 1.00 [0.05, 18.91] |] |
| Lee et al, 2014 | 11 | 78 | 6 | 21 | 86.9% | 0.41 [0.13, 1.29] | aj <u> </u> |
| Liu et al, 2012 | 0 | 14 | 10 | 50 | 0.0% | 0.13 [0.01, 2.42] | 2] |
| Total (95% CI) | | 84 | | 24 | 100.0% | 0.46 [0.16, 1.34] | |
| Total events | 15 | | 8 | | | | |
| Heterogeneity: Tau ² = 0.00; Chi ² = 0.31, df = 1 (P = 0.58); I ² = 0% | | | | | | | |
| Test for overall effect: | | | | | | | 0.01 0.1 1 10 100 Favours surgery <3 days Favours surgery >3 days |

| | Surgery within | 3 days | Surgery after | r 3 days | | Odds Ratio | Odds Ratio |
|--------------------------|--------------------|--------|---------------|----------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% Cl |
| Knutson et al, 1983 | 4 | 6 | 2 | 3 | 0.0% | 1.00 [0.05, 18.91] | |
| Lee et al, 2014 | 11 | 78 | 6 | 21 | 0.0% | 0.41 [0.13, 1.29] | |
| Liu et al, 2012 | 0 | 14 | 10 | 50 | 100.0% | 0.13 [0.01, 2.42] 👎 | |
| Total (95% CI) | | 14 | | 50 | 100.0% | 0.13 [0.01, 2.42] - | |
| Total events | 0 | | 10 | | | | |
| Heterogeneity: Not ap | | | | | | H | 0.01 0.1 1 10 100 |
| Test for overall effect: | Z = 1.36 (P = 0.17 | 7 | | | | 0 | Favours surgery <3 days Favours surgery >3 days |

Hospital presentation within 3 days after onset symptoms - mortality as outcome

| | Presentation within | 1 3days | Presentation afte | r 3 days | | Odds Ratio | Odds Ratio |
|-----------------------------------|-------------------------------------|-------------|-------------------|----------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Barupal et al, 2019 | 7 | 15 | 9 | 35 | 19.0% | 2.53 [0.71, 8.97] | |
| Boyer et al, 2009 | 25 | 65 | 18 | 41 | 22.6% | 0.80 [0.36, 1.77] | |
| Catena et al, 2004 | 1 | 4 | 6 | 7 | 8.3% | 0.06 [0.00, 1.23] | ← → → → → → → → → → → → → → → → → → → → |
| Ferretti et al, 2017 | 3 | 14 | 0 | 6 | 8.2% | 3.96 [0.18, 89.19] | |
| Huang et al, 2008 | 1 | 14 | 2 | 2 | 7.1% | 0.02 [0.00, 0.72] | ← → |
| Knutson et al, 1983 | 5 | 8 | 1 | 1 | 7.1% | 0.52 [0.02, 16.83] | |
| Lee et al, 2014 | 12 | 90 | 5 | 9 | 17.6% | 0.12 [0.03, 0.52] | |
| Yu et al, 2004 | 1 | 6 | 2 | 9 | 10.1% | 0.70 [0.05, 10.01] | |
| Total (95% CI) | | 216 | | 110 | 100.0% | 0.49 [0.16, 1.44] | |
| Total events | 55 | | 43 | | | | |
| Heterogeneity: Tau ² = | : 1.19; Chi ² = 17.11, d | f= 7 (P = 0 | | | | | |
| Test for overall effect: | Z = 1.30 (P = 0.19) | | | | | | 0.01 0.1 1 10 100 Favours surgery <3 days Favours surgrery >3 days |

Subgroup analysis: High-quality studies

| | Presentation withi | n 3days | Presentation afte | r 3 days | | Odds Ratio | Odds Ratio |
|-----------------------------------|-----------------------------------|-------------|-------------------|----------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% CI |
| Barupal et al, 2019 | 7 | 15 | 9 | 35 | 32.2% | 2.53 [0.71, 8.97] | |
| Boyer et al, 2009 | 25 | 65 | 18 | 41 | 37.8% | 0.80 [0.36, 1.77] | _ |
| Catena et al, 2004 | 1 | 4 | 6 | 7 | 0.0% | 0.06 [0.00, 1.23] | |
| Ferretti et al, 2017 | 3 | 14 | 0 | 6 | 0.0% | 3.96 [0.18, 89.19] | |
| Huang et al, 2008 | 1 | 14 | 2 | 2 | 0.0% | 0.02 [0.00, 0.72] | |
| Knutson et al, 1983 | 5 | 8 | 1 | 1 | | Not estimable | |
| Lee et al, 2014 | 12 | 90 | 5 | 9 | 30.0% | 0.12 [0.03, 0.52] | _ |
| Yu et al, 2004 | 1 | 6 | 2 | 9 | 0.0% | 0.70 [0.05, 10.01] | |
| Total (95% CI) | | 170 | | 85 | 100.0% | 0.66 [0.15, 2.83] | |
| Total events | 44 | | 32 | | | | |
| Heterogeneity: Tau ² = | 1.29; Chi ² = 9.56, df | = 2 (P = 0. | 008); I² = 79% | | | | |
| Test for overall effect: | Z = 0.56 (P = 0.58) | · | | | | | 0.01 0.1 1 10 100 Favours surgery <3 days Favours surgery >3 days |

Subgroup analysis: Studies published ≥2009

| | Presentation withi | n 3days | Presentation after | 3 days | | Odds Ratio | Odds Ratio |
|--------------------------|-----------------------------------|-------------|--------------------|--------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% Cl |
| Barupal et al, 2019 | 7 | 15 | 9 | 35 | 28.2% | 2.53 [0.71, 8.97] | |
| Boyer et al, 2009 | 25 | 65 | 18 | 41 | 33.5% | 0.80 [0.36, 1.77] | |
| Catena et al, 2004 | 1 | 4 | 6 | 7 | 0.0% | 0.06 [0.00, 1.23] | |
| Ferretti et al, 2017 | 3 | 14 | 0 | 6 | 12.2% | 3.96 [0.18, 89.19] | |
| Huang et al, 2008 | 1 | 14 | 2 | 2 | 0.0% | 0.02 [0.00, 0.72] | |
| Knutson et al, 1983 | 5 | 8 | 1 | 1 | 0.0% | 0.52 [0.02, 16.83] | |
| Lee et al, 2014 | 12 | 90 | 5 | 9 | 26.1% | 0.12 [0.03, 0.52] | |
| Yu et al, 2004 | 1 | 6 | 2 | 9 | 0.0% | 0.70 [0.05, 10.01] | |
| Total (95% CI) | | 184 | | 91 | 100.0% | 0.82 [0.22, 3.09] | |
| Total events | 47 | | 32 | | | | |
| Heterogeneity: Tau² = | 1.20; Chi ² = 10.64, d | f= 3 (P = 0 |).01); I² = 72% | | | | |
| Test for overall effect: | Z = 0.29 (P = 0.78) | | | | | | 0.01 0.1 1 10 100 Favours surgery <3 days Favours surgrery >3 days |

Subgroup analysis: Studies without limitation on affected body region by NSTI

| | Presentation withi | n 3days | Presentation afte | r 3 days | | Odds Ratio | Odds Ratio |
|-----------------------------------|-----------------------------------|-------------|-----------------------------|----------|--------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Barupal et al, 2019 | 7 | 15 | 9 | 35 | 27.6% | 2.53 [0.71, 8.97] | |
| Boyer et al, 2009 | 25 | 65 | 18 | 41 | 0.0% | 0.80 [0.36, 1.77] | |
| Catena et al, 2004 | 1 | 4 | 6 | 7 | 15.1% | 0.06 [0.00, 1.23] | ← ■+ |
| Ferretti et al, 2017 | 3 | 14 | 0 | 6 | 0.0% | 3.96 [0.18, 89.19] | |
| Huang et al, 2008 | 1 | 14 | 2 | 2 | 0.0% | 0.02 [0.00, 0.72] | |
| Knutson et al, 1983 | 5 | 8 | 1 | 1 | 13.3% | 0.52 [0.02, 16.83] | |
| Lee et al, 2014 | 12 | 90 | 5 | 9 | 26.3% | 0.12 [0.03, 0.52] | |
| Yu et al, 2004 | 1 | 6 | 2 | 9 | 17.6% | 0.70 [0.05, 10.01] | |
| Total (95% CI) | | 123 | | 61 | 100.0% | 0.41 [0.08, 2.13] | |
| Total events | 26 | | 23 | | | | |
| Heterogeneity: Tau ² = | 2.10; Chi ² = 11.84, d | f= 4 (P = 0 | 0.02); I ² = 66% | | | | |
| Test for overall effect: | | | | | | | 0.01 0.1 1 10 100 Favours surgery <3 days Favours surgery >3 days |

| | Presentation within | 1 3days | Presentation afte | r 3 days | | Odds Ratio | Odds Ratio |
|-----------------------------------|-------------------------------------|-------------|-------------------|----------|--------|---------------------|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% Cl | M-H, Random, 95% Cl |
| Barupal et al, 2019 | 7 | 15 | 9 | 35 | 29.6% | 2.53 [0.71, 8.97] | |
| Boyer et al, 2009 | 25 | 65 | 18 | 41 | 41.5% | 0.80 [0.36, 1.77] | |
| Catena et al, 2004 | 1 | 4 | 6 | 7 | 8.8% | 0.06 [0.00, 1.23] | · · · · · · · · · · · · · · · · · · · |
| Ferretti et al, 2017 | 3 | 14 | 0 | 6 | 8.8% | 3.96 [0.18, 89.19] | |
| Huang et al, 2008 | 1 | 14 | 2 | 2 | 0.0% | 0.02 [0.00, 0.72] | |
| Knutson et al, 1983 | 5 | 8 | 1 | 1 | 0.0% | 0.52 [0.02, 16.83] | |
| Lee et al, 2014 | 12 | 90 | 5 | 9 | 0.0% | 0.12 [0.03, 0.52] | |
| Yu et al, 2004 | 1 | 6 | 2 | 9 | 11.3% | 0.70 [0.05, 10.01] | |
| Total (95% CI) | | 104 | | 98 | 100.0% | 1.01 [0.37, 2.74] | |
| Total events | 37 | | 35 | | | | |
| Heterogeneity: Tau ² = | 0.47; Chi ² = 6.53, df = | = 4 (P = 0. | | | | | |
| Test for overall effect: | | , | | | | | 0.01 0.1 1 10 100 Favours surgery <3 days Favours surgrery >3 days |
| | | | | | | | Favours surgery <5 days Favours surgrery <5 days |