Knee Donor-Site Morbidity Following Autologous Osteochondral Transplantation for Osteochondral Lesions of the Talus: A Systematic Review and Meta-Analysis

Yoshiharu Shimozono, MD, Dexter Seow, MB, BCh, Youichi Yasui, MD, PhD, Kara Fields, MPH, John G. Kennedy, MD, MCh, MMSc, FFSEM, FRCS(Orth)

NYU Langone Health, NYU Orthopedic Hospital
Yoshiharu Shimozono, MD

I have no financial conflict to disclose.
Introduction

- Autologous osteochondral transplantation (AOT) for osteochondral lesions of the talus (OLT)
  - Good to Excellent at mid-term
  - 90% of professional athletes return to sports
- Concern - Knee donor site morbidity (DSM)
  - Reported to range from 0%- 54.5%

Risk of Knee DSM
- Not well established
- Heterogeneous studies with *loss to follow-up*

Valderrabano V, AJSM 2009, Fraser FAI 2016
Purpose

• To evaluate the proportion of knee DSM after AOT for OLT by

(1) meta-analysis in the best-case scenario in which **NO** patients lost to follow-up were assumed to have DSM

(2) meta-analysis in the worst-case scenario in which **ALL** patients lost to follow-up were assumed to have DSM

(3) present the characteristics of studies associated with the reporting of DSM
Methods

- A systematic review of MEDLINE, EMBASE, and Cochrane Library databases was performed based on the PRISAM guideline

✓ Inclusion criteria
  - Clinical studies reported knee DSM after AOT for OLT
  - Follow-up > 1 year
  - Published in a peer-reviewed journal

✓ Exclusion criteria
  - Review articles, Case reports, Cadaver studies, Animal studies

- Assessment of evidence
  - Previously published case series quality checklist
  - The checklist was answered with either “yes”, “no”, “partial” or “unclear”.
  - Mean total number of responses of either “yes” or “partial” was 6.4 (4 to 10)
Methods

• Characteristics
  – Lesion size, donor-site for the grafts, diameter and number of the grafts

• Use random effects models to estimate the risk of knee DSM
  – Either assuming no patients lost to follow-up had DSM, or all patients lost to follow-up had DSM

• Use Multivariable meta-regression to estimate the association between study characteristics and the observed risk of DSM
Results

- Total 26 studies with 915 ankles (904 patients)
  - Mean age 34.2 ± 7.4 years
  - Mean follow-up 43.8 ± 24.7 months (16 to 120)
- 12 studies reported loss to follow-up
  - 32 patients (35 ankles) were reported in total
Results

- Mean OLT size: 142.7 mm²
- Mean number of grafts: 1.7
- Mean diameter of grafts: 9.9 mm
- Donor-site
  - Lateral femoral condyle (19 studies)
  - Medical femoral condyle (2 studies)
  - Notch of femoral trochlea (1 study)

- DSM definition
  - No study reported
  - Pain, Stiffness, instability, crepitus, discomfort

- Outcome Measures of the knee
  - 7 different scoring systems reported in 9 studies
  - Lysholm, IKDC, Cincinnati, Bandi, HSS, Kujala, VAS
Results

**Best-case analysis**
- If no patients lost to follow-up had knee DSM
  - 6.7% (95% CI 2.8 – 11.8%, $I^2 = 82.1\%$)

**Worst-case analysis**
- If all patients lost to follow-up had knee DSM
  - 10.8% (95% CI 4.8 – 18.3%, $I^2 = 88.7\%$)

- There was a negative association between study sample size and rate of DSM ($\beta$ [95% CI]: -0.26 [-0.39 to -0.12], $p < 0.001$)
  - Larger studies tend to report lower rate of knee DSM

- Therefore, *subgroup analysis was performed by sample size.*
Results

- If no patients lost to follow-up had knee DSM
  - N > 30: 2.8% [95% CI, 1.2 to 5.0]

- If all patients lost to follow-up had knee DSM
  - N > 30: 5.0% [95% CI, 5.8 to 29.4]

Author, Year | Events/Total | Donor-Site Morbidity (%) [95% CI]
--- | --- | ---
N ≥ 30
- Balthasar et al., 2005 [4] | 1/43 | 2.3 [0.0, 9.7]
- de l'Escalopier et al., 2015 [5] | 6/37 | 16.2 [5.8, 30.3]
- Erne et al., 2012 [7] | 2/32 | 6.3 [0.1, 17.9]
- Flynn et al., 2016 [8] | 2/87 | 2.3 [0.0, 6.8]
- Fraser et al., 2016 [10] | 2/40 | 5.0 [0.1, 14.5]
- Fraser et al., 2016 [9] | 4/36 | 11.1 [2.5, 38.9]
- Halleen et al., 2014 [15] | 0/42 | 0.0 [0.0, 4.1]
- Hangody et al., 2003 [16] | 1/76 | 1.3 [0.0, 5.6]
- Kennedy et al., 2011 [19] | 3/72 | 4.2 [0.5, 10.3]
- Kim et al., 2012 [20] | 0/69 | 0.0 [0.0, 2.5]
- Ross et al., 2016 [28] | 2/76 | 2.6 [0.0, 7.9]
- Schoettle et al., 2002 [29] | 0/39 | 0.0 [0.0, 4.4]
- Scranton et al., 2000 [31] | 1/50 | 2.0 [0.0, 8.4]
- Woelke et al., 2013 [34] | 2/96 | 5.6 [0.1, 16.0]

Random-Effects Model for Subgroup
Q = 24.86, df = 13, p = 0.024, I² = 47.6%

N < 30
- Ahmad et al., 2016 [1] | 6/20 | 30.0 [11.6, 52.2]
- Al-Shahki et al., 2002 [2] | 6/19 | 42.0 [26.3, 65.2]
- Gobbi et al., 2006 [12] | 0/12 | 0.0 [0.0, 13.9]
- Haasper et al., 2008 [14] | 3/14 | 21.4 [3.2, 47.3]
- Largey et al., 2009 [21] | 1/5 | 20.0 [0.0, 67.5]
- Lee et al., 2003 [22] | 2/18 | 11.1 [0.2, 30.6]
- Reddy et al., 2007 [27] | 6/15 | 40.0 [16.3, 68.2]
- Scranton et al., 2001 [32] | 0/10 | 0.0 [0.0, 16.5]
- Valderrabano et al., 2009 [33] | 6/21 | 28.6 [10.9, 50.0]
- Yoon et al., 2014 [35] | 0/22 | 0.0 [0.0, 7.7]
- Zhu et al., 2016 [36] | 0/13 | 0.0 [0.0, 12.8]

Random-Effects Model for Subgroup
Q = 43.63, df = 11, p < 0.001, I² = 74.9%

Random-Effects Model for All Studies
Q = 158.13, df = 25, p < 0.001, I² = 82.1%

Author, Year | Events/Total | Donor-Site Morbidity (%) [95% CI]
--- | --- | ---
N ≥ 30
- Balthasar et al., 2005 [4] | 1/43 | 2.3 [0.0, 9.7]
- de l'Escalopier et al., 2015 [5] | 6/37 | 16.2 [5.8, 30.3]
- Erne et al., 2012 [7] | 2/32 | 6.3 [0.1, 17.9]
- Flynn et al., 2016 [8] | 2/87 | 2.3 [0.0, 6.8]
- Fraser et al., 2016 [10] | 2/40 | 5.0 [0.1, 14.5]
- Fraser et al., 2016 [9] | 4/36 | 11.1 [2.5, 38.9]
- Halleen et al., 2014 [15] | 0/42 | 0.0 [0.0, 4.1]
- Hangody et al., 2003 [16] | 1/76 | 1.3 [0.0, 5.6]
- Kennedy et al., 2011 [19] | 3/72 | 4.2 [0.5, 10.3]
- Kim et al., 2012 [20] | 0/69 | 0.0 [0.0, 2.5]
- Ross et al., 2016 [28] | 2/76 | 2.6 [0.0, 7.9]
- Schoettle et al., 2002 [29] | 0/39 | 0.0 [0.0, 4.4]
- Scranton et al., 2000 [31] | 1/50 | 2.0 [0.0, 8.4]
- Woelke et al., 2013 [34] | 2/96 | 5.6 [0.1, 16.0]

Random-Effects Model for Subgroup
Q = 51.44, df = 13, p = 0.024, I² = 74.5%

N < 30
- Ahmad et al., 2016 [1] | 6/20 | 30.0 [11.6, 52.2]
- Al-Shahki et al., 2002 [2] | 6/19 | 42.0 [26.3, 65.2]
- Gobbi et al., 2006 [12] | 0/12 | 0.0 [0.0, 13.9]
- Haasper et al., 2008 [14] | 3/14 | 21.4 [3.2, 47.3]
- Largey et al., 2009 [21] | 1/5 | 20.0 [0.0, 67.5]
- Lee et al., 2003 [22] | 2/18 | 11.1 [0.2, 30.6]
- Reddy et al., 2007 [27] | 6/15 | 40.0 [16.3, 68.2]
- Scranton et al., 2001 [32] | 0/10 | 0.0 [0.0, 16.5]
- Valderrabano et al., 2009 [33] | 6/21 | 28.6 [10.9, 50.0]
- Yoon et al., 2014 [35] | 0/22 | 0.0 [0.0, 7.7]
- Zhu et al., 2016 [36] | 0/13 | 0.0 [0.0, 12.8]

Random-Effects Model for Subgroup
Q = 78.19, df = 11, p < 0.001, I² = 83.4%

Random-Effects Model for All Studies
Q = 171.76, df = 25, p < 0.001, I² = 88.7%
Limitations

- Very difficult to assess accurately loss to follow-up in the studies
- 12 studies did not comment on loss to follow-up
  - May result in underestimation of knee DSM
- Selection and assessor bias
  - Also may result in the reported incidence of DSM being lower than the actual rate
- Short term follow-up
  - An increase in DSM may become evident in time if the harvesting of cartilage results in arthritic changes

- High heterogeneity
  - Unexplainable by variability in sample size, age, study design, or follow-up time
- No studies described the definition of knee DSM
The estimated proportion of knee DSM ranged from 6.7% to 10.8% at short- to mid-term follow-up (< 5 years).

However, subgroup analysis demonstrated that larger studies (n>30) estimated lower DSM risk (<5.0%) than smaller studies.

The estimated should be interpreted in light of the fact that nearly half of the included studies did not report on loss to follow-up.

Future meta-analysis that includes larger prospective studies with longer-term and more complete follow-up is needed.
References


