Investigating Muscle Enlargement and Motility Restriction in Orbital Fracture Patients

Final Report

Hannah Steinberg | Gabriel Pham | Peiyuan Lee | Mari Yamamoto | Jasmine Yung | Bella Gordon

Abstract

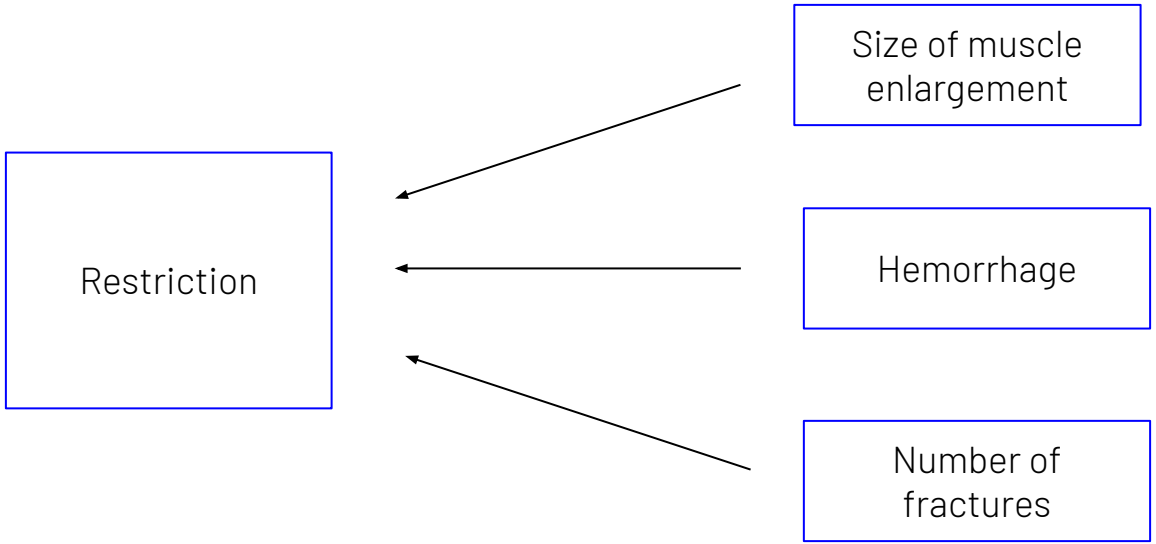
Orbital fractures can lead to significant complications affecting ocular function, including muscle enlargement (percent increase in surface area of the eye muscles between an eye with a fracture and an eye without) and restricted motility (confined gaze movements). Previous literature has not explored if muscle enlargement is associated with muscle restriction, so the present study investigates the relationship. A dataset of N=123 was collected and analyzed using a variety of methods. The muscle enlargement variables alone did not consistently show significant differences between restricted and unrestricted groups in hypothesis testing. However, model-based approaches (e.g., Random Forest, Logistic Regression) consistently identified a Retrobulbar hemorrhage in the fractured eye as an important predictor of restriction in gaze movements.

Problem Statement

- Is there an association between motility restriction and muscle enlargement in patients with orbital fractures?

- What are the variables that influence muscle restriction?

Schematic


Size of muscle enlargement
Restriction
Hemorrhage
Number of fractures

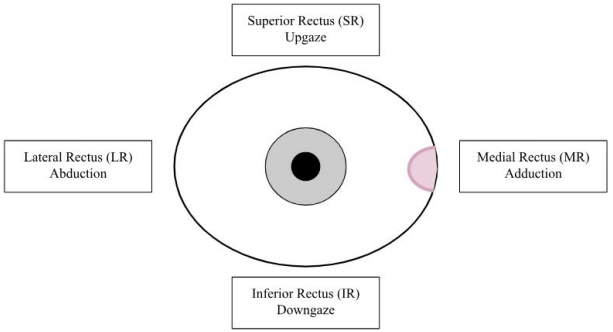
Variables

Demographic Variables:

- Patient_ID
- Sex
- Age
- Laterality
  - OS → left eye fractured; OD → right eye fractured

Eye-Related Variables:

- Muscle Surface Area (mm)
  - One variable per muscle
- Difference in Muscle Surface Area between Control and Fracture Eye (%)
  - > 67% → fracture eye muscle is enlarged
  - One variable per eye (CSA_##)
- Muscle Size (binomial)
  - If CSA for that direction > 75% → “large” (1), otherwise “normal” (0)
- Muscle BI (binomial)
  - Is any muscle in the fracture eye enlarged?
- Fracture Type (binomial)
  - One variable per direction; if the fracture eye was fractured in that direction → 1
- Sum Fracture (numerical)
  - Sums up the fracture type variable for each person
- Gaze (°)
  - One variable per direction
  - > 67% → fracture eye is restricted in that direction
- Restriction (binomial)
  - One variable for if there is restriction in any direction and one variable for each individual direction
- Global Motility (binomial)
  - Is there restriction in every direction?
- Retrobulbar Hemorrhage (binomial)
  - Is there bleeding behind the fractured eye?
- Emphysema (Binomial)
  - Is there air trapped in the eye muscles or lid?



Data Preparation:

Exploratory Checks:

- str() and glimpse() used to verify structure and variable types
- colSums(is.na(...)) used to check for missing values

```
tibble [123 × 48] (S3: tbl_df/tbl/data.frame)
 $ Patient_ID            : chr [1:123] "KL_1" "KL_2" "KL_3" "KL_4" ...
 $ Age                   : num [1:123] 35 75 41 28 22 46 21 14 45 21 ...
 $ Sex                   : Factor w/ 2 levels "0","1": 1 1 1 1 1 1 1 1 1 1 ...
 $ Laterality            : Factor w/ 2 levels "OD","OS": 2 2 1 2 1 1 1 2 2 2 ...
 $ Restriction           : Factor w/ 2 levels "0","1": 1 1 1 2 1 2 2 2 2 1 ...
 $ Global_Motility       : num [1:123] 0 0 0 0 0 0 0 0 0 0 ...
 $ Upgaze                : num [1:123] 45 45 45 35 45 45 45 30 45 45 ...
```

Handling Missing Values:

- Global_Motility: NAs replaced with 0 (assumed no movement)
- NAs for retrobulbar hemorrhage and other variables: missing because they were never recorded, no changes made

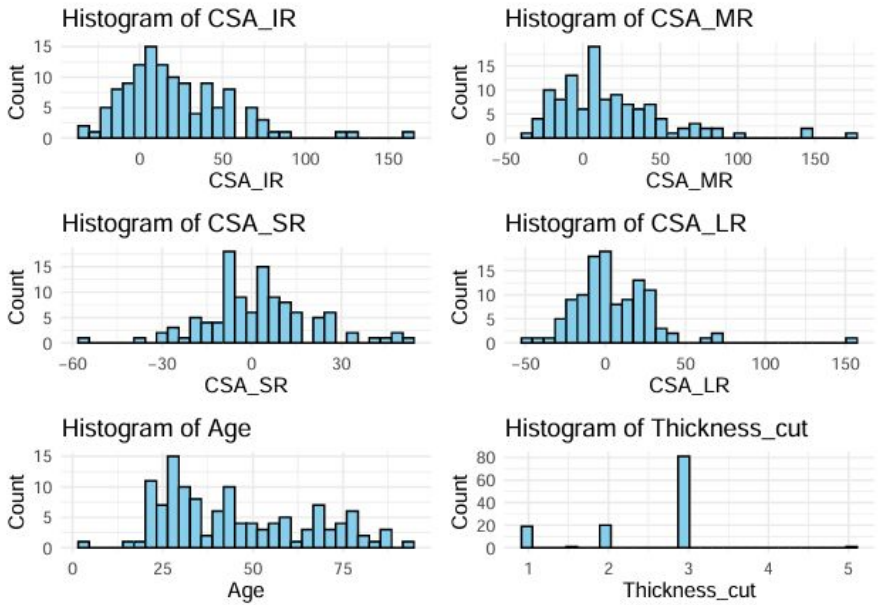
Variable Conversion:

- Converted the following variables to factors:
  - Sex, Laterality, Restriction, Floor, Roof, Lateral, Medial
  - Retrobulbar_hemorrhage, Emphysema
  - restrict_Up, restrict_Down, restrict_AB, restrict_AD
  - SR_size, IR_size, MR_size, LR_size
  - Global_Motility, sum_fracture, muscle_bi
- Converted the following variables into ordinal factors:
  - sum_fracture: converted to ordered factor (levels 1–4)
  - All _size variables converted to ordered factor (normal < large)

```
  Patient_ID            Age              Sex          Laterality  Restriction Global_Motility      Upgaze          Downgaze
 Length:123         Min.   : 3.00   0:93   OD:57        0:64        Min.   :0.00000   Min.   : 0.00   Min.   : 0.00
 Class :character   1st Qu.:28.50   1:30   OS:66        1:59        1st Qu.:0.00000   1st Qu.:30.00   1st Qu.:45.00
 Mode  :character   Median :41.00                                   Median :0.00000   Median :45.00   Median :45.00
                    Mean   :45.33                                   Mean   :0.06504   Mean   :35.85   Mean   :41.19
                    3rd Qu.:61.50                                   3rd Qu.:0.00000   3rd Qu.:45.00   3rd Qu.:45.00
                    Max.   :93.00                                   Max.   :1.00000   Max.   :45.00   Max.   :50.00
                                                                                                      NA's   :1
   ADduction        ABduction       Floor   Roof     Lateral  Medial  Retrobulbar_hemorrhage Emphysema Thickness_cut        RSR
 Min.   : 0.00   Min.   : 0.00   0:24   0:108   0:98    0:68   0   :77                0   :78   Min.   :0.940   Min.   :0.1400
 1st Qu.:45.00   1st Qu.:35.00   1:99   1: 15   1:25    1:55   1   :11                1   :43   1st Qu.:2.000   1st Qu.:0.2300
 Median :45.00   Median :45.00                                 NA's:35                NA's: 2   Median :3.000   Median :0.2700
 Mean   :41.52   Mean   :39.43                                                                  Mean   :2.528   Mean   :0.2741
 3rd Qu.:45.00   3rd Qu.:45.00                                                                 3rd Qu.:3.000   3rd Qu.:0.3200
 Max.   :45.00   Max.   :45.00                                                                 Max.   :5.000   Max.   :0.4300
 NA's   :1       NA's   :1                                                                     NA's   :1       NA's   :12
```

Distributions of Muscle Size, Age, and Thickness Cut

Goal recap: Assess whether extraocular muscle size/enlargement is associated with motility restriction in patients with orbital fractures - particularly when no entrapment is present.



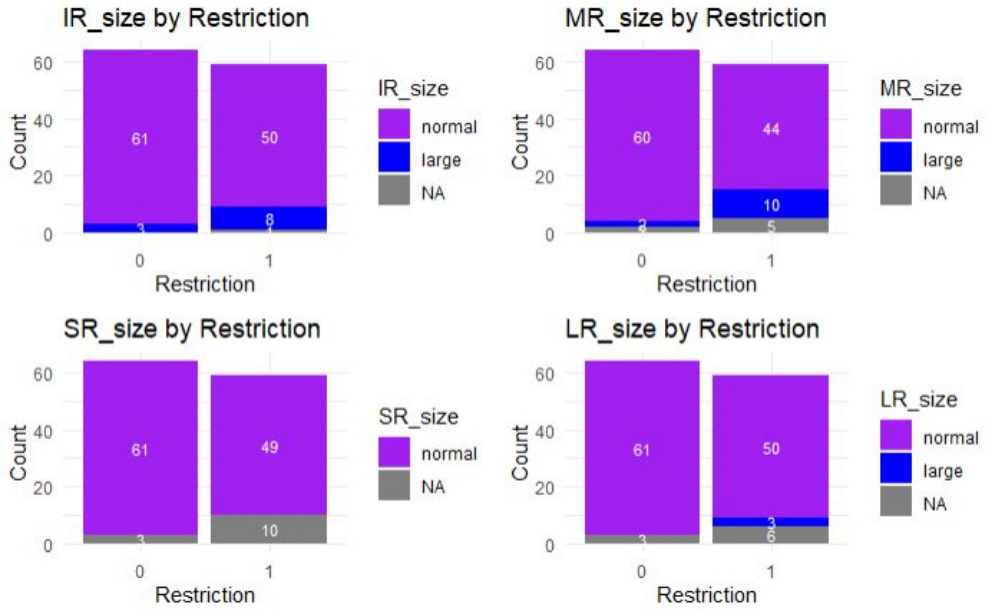
CSA_IR, CSA_MR, CSA_SR, CSA_LR show positively skewed distributions with a few outliers, which is common in medical measurements. Age is widely distributed. Thickness cut is mostly constant at 3.
Were calculated using n = 109 complete cases out of a total of 123 patients.

Muscle Enlargement by Restriction Status

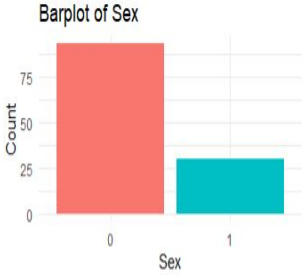
MR_size and IR_size: a notable number of "large" observations occur in restricted patients.

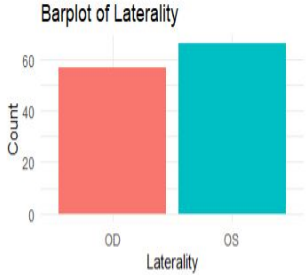
SR_size and LR_size: very few “large” entries, and no apparent association with restriction.

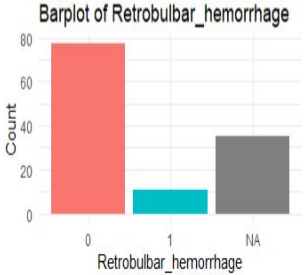
Suggest that MR and IR muscles are more frequently enlarged in restricted patients.

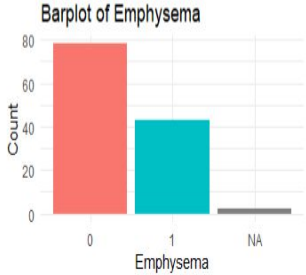


Frequencies of variables

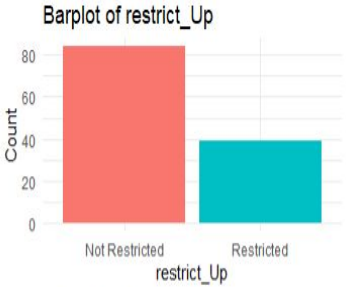


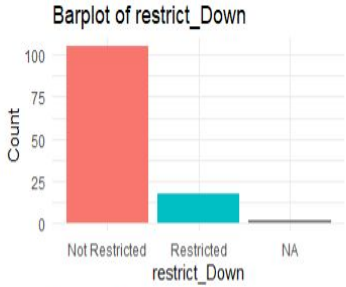


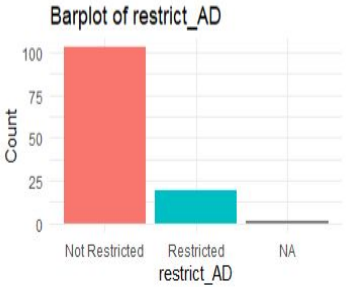


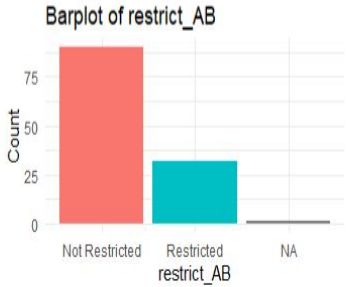


Sex: majority male.
Laterality: distribution between left and right eyes is fairly even.
Retrobulbar hemorrhage: Most do not have hemorrhage
4 gaze directions: most patients are not restricted, highlights that restriction is present but not dominant.

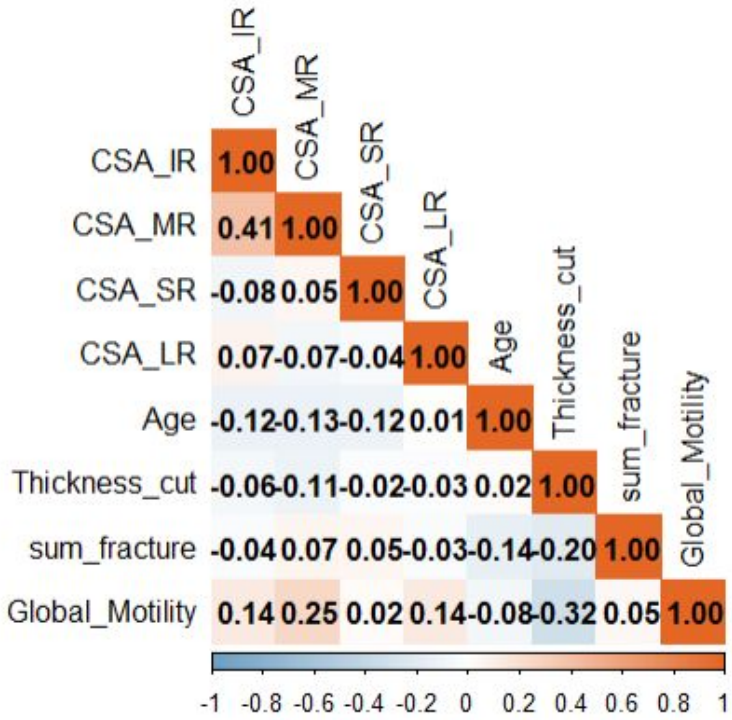








EDA - Correlation Matrix



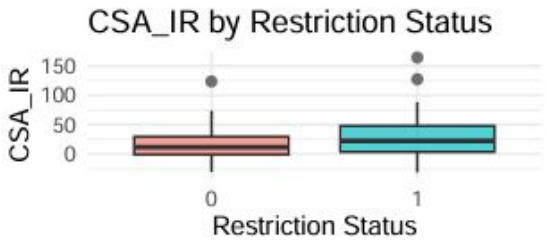
Muscle Size (CSA_MR) and Tissue Thickness have the strongest links to eye movement problems (Global_Motility).
So, when the medial rectus muscle is larger or the tissue is thicker, people are more likely to have difficulty moving their eye.
However, as the histogram above, Tissue Thickness most fall in 3, hence this signal might be weak or misleading.

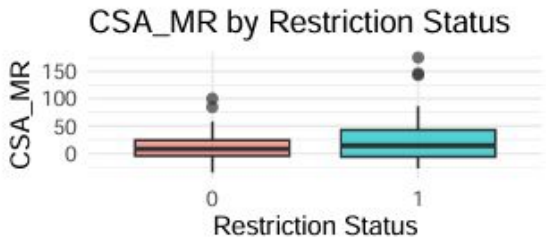
Other muscle sizes (like CSA_IR, CSA_SR, CSA_LR) don't seem to have a big effect on eye movement on their own as their numbers are close to 0.

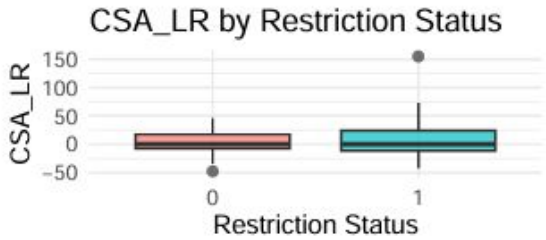
Bone fractures (sum_fracture) don't show a strong connection to eye movement either.

Age has a small effect - older people may have slightly smaller muscles.

Boxplots by Restriction Status for CSA_* and AgeC

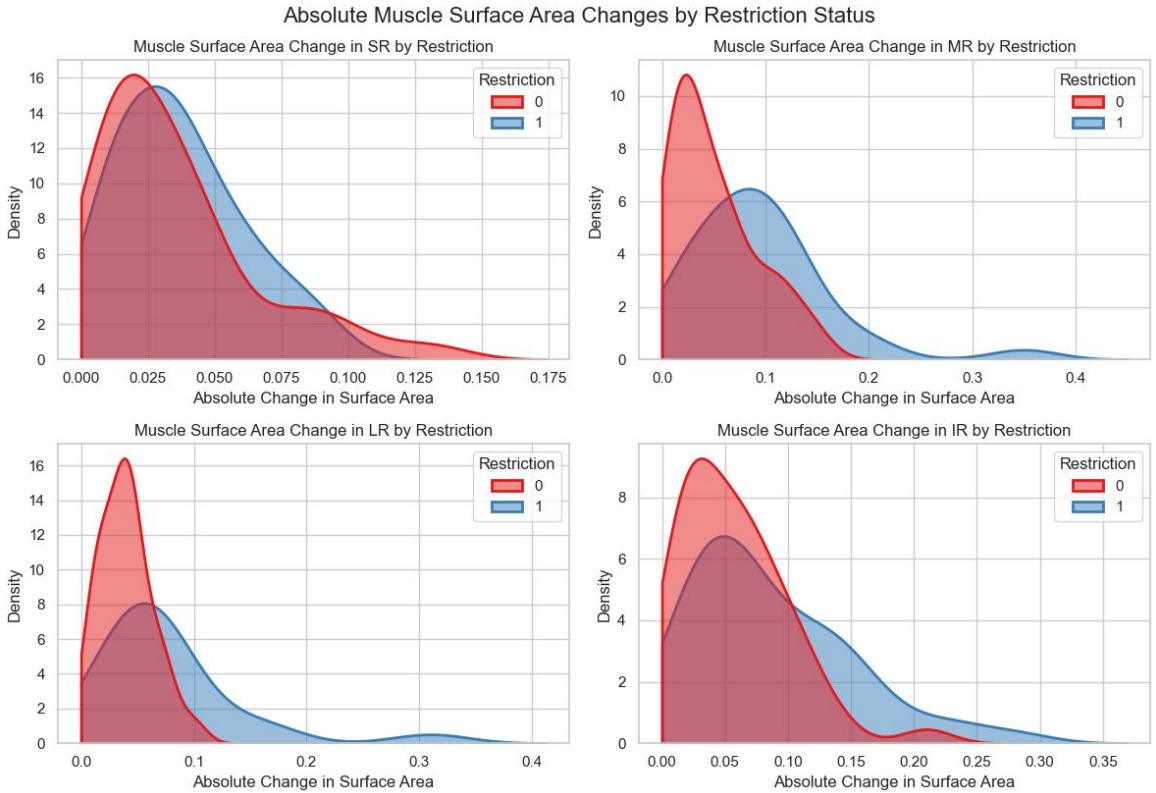






CSA_IR and MR: Median values are slightly higher in the restricted group
SR and LR: Don’t show much strong patterns.
Age: Restricted group is clearly younger than non restricted group

Hypothesis Test: Overall Restriction



- We are interested in determining if there is an association between muscle enlargement and motility restriction
- Upon visual inspection, we can see that the distribution of the absolute change in muscle surface areas is not normal, and there isn't a noticeable difference between the unrestricted and restricted groups

Hypothesis Test: Overall Restriction

Shapiro-Wilk Test to test for Normality

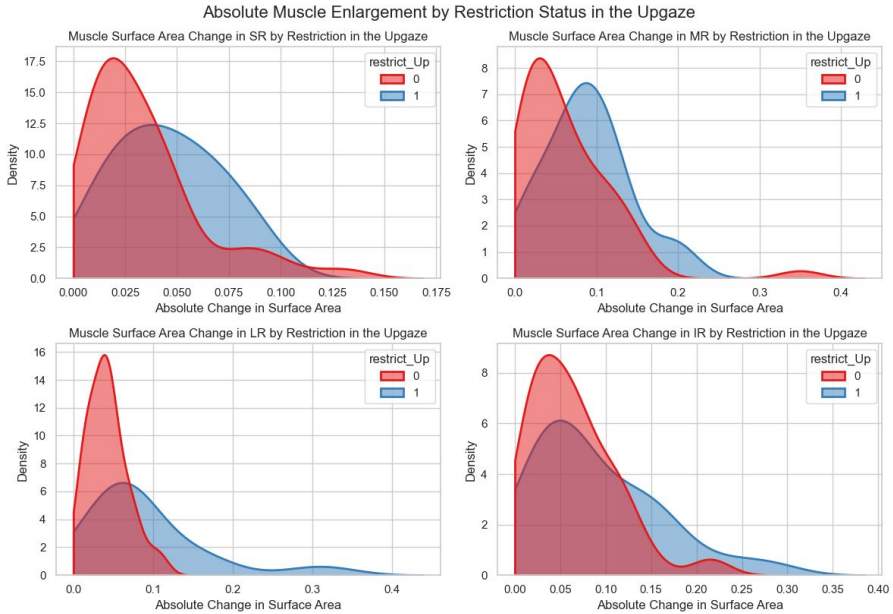
Muscle	P-value for Non-restricted Group	P-value for Restricted Group	Result
abs_SR	2.2280246e-05	0.0674868	Not normal
abs_MR	0.0001703	0.0003874	Not normal
abs_LR	0.0510635	5.5553661e-05	Not normal
abs_IR	0.00056726	0.0012440	Not normal

Mann Whitney-U Test

Muscle	P-value	Result
abs_SR	0.4633544515848277	Fail to reject null hypothesis
abs_MR	**0.0008646921960961505**	**Reject the null hypothesis**
abs_LR	0.005176195016496183	Fail to reject null hypothesis
abs_IR	0.03049057887349152	Fail to reject null hypothesis

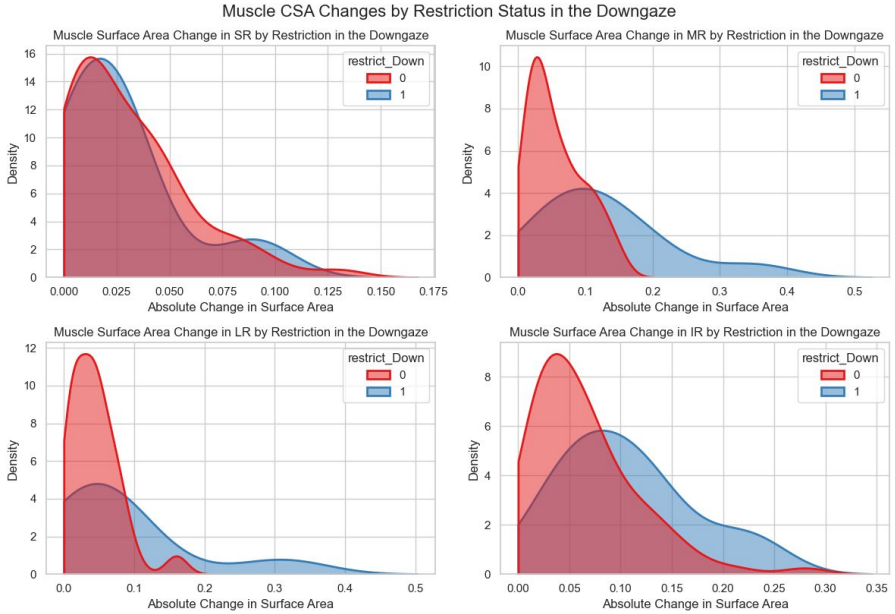
From the hypothesis test, we concluded that muscle enlargement, with the exception of enlargement in the medial rectus, does not contribute significantly to overall motility restriction.

Hypothesis Test: Restriction in the Upgaze



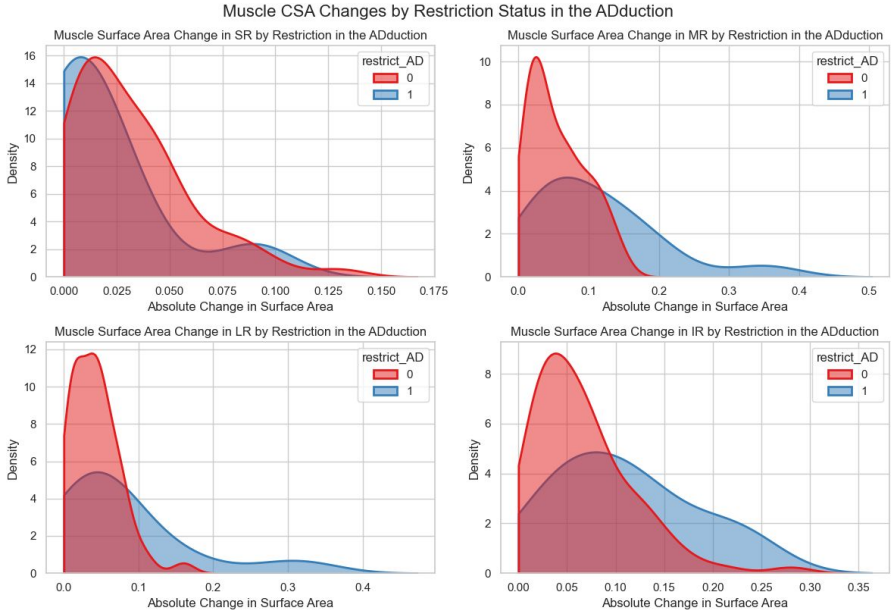
Muscle	p-value	Result
abs_SR	0.1142021369317709	Fail to reject null hypothesis
abs_MR	0.0189344458708622	Fail to reject null hypothesis
abs_LR	0.0033072155576550567	Fail to reject null hypothesis
abs_IR	0.12405316261909627	Fail to reject null hypothesis

Hypothesis Test: Restriction in the Downgaze



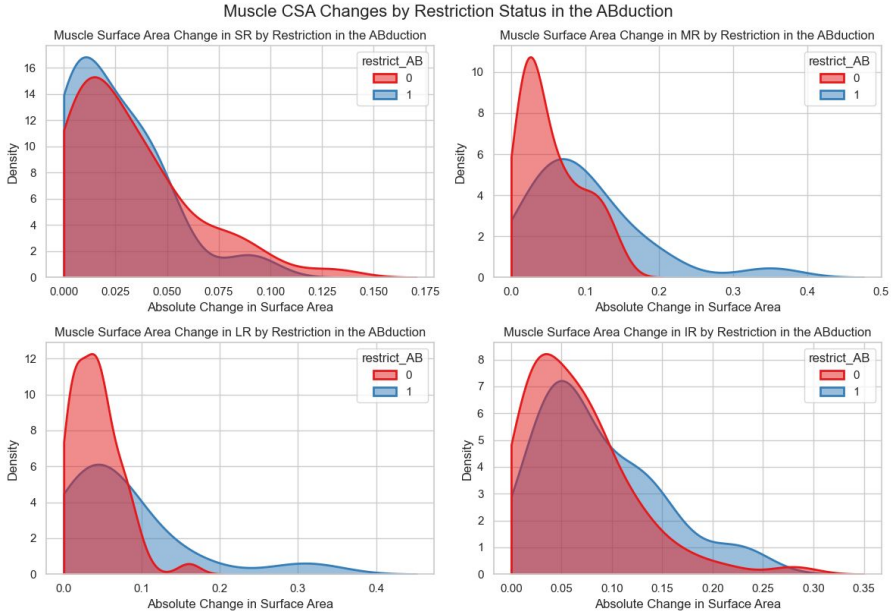
Muscle	p-value	Result
abs_SR	0.2586811514855196	Fail to reject the null hypothesis
abs_MR	0.011217020353296692	Fail to reject the null hypothesis
abs_LR	0.22600741241234612	Fail to reject the null hypothesis
abs_IR	0.018615070289110285	Fail to reject the null hypothesis

Hypothesis Test: Restriction in the ADduction



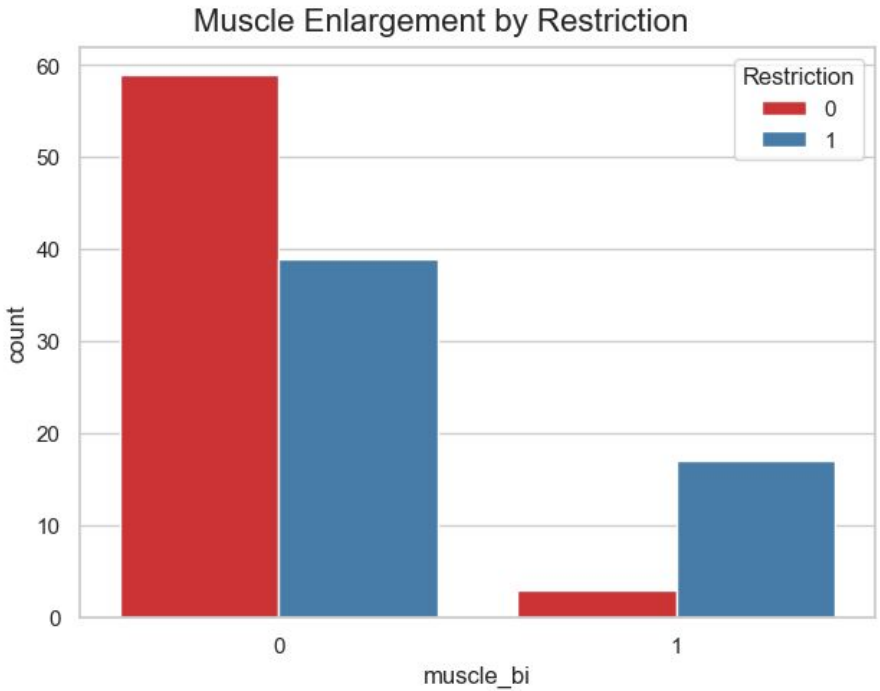
Muscle	p-value	Result
abs_SR	0.613362599966701	Fail to reject the null hypothesis
abs_MR	0.004821338581428693	Fail to reject the null hypothesis
abs_LR	0.23544113033377279	Fail to reject the null hypothesis
abs_IR	0.023124591017566986	Fail to reject the null hypothesis

Hypothesis Test: Restriction in the ABduction



Muscle	p-value	Result
abs_SR	0.4996761965894939	Fail to reject the null hypothesis
abs_MR	0.0095174950787319	Fail to reject the null hypothesis
abs_LR	0.0798096608727745	Fail to reject the null hypothesis
abs_IR	0.0692369415877943	Fail to reject the null hypothesis

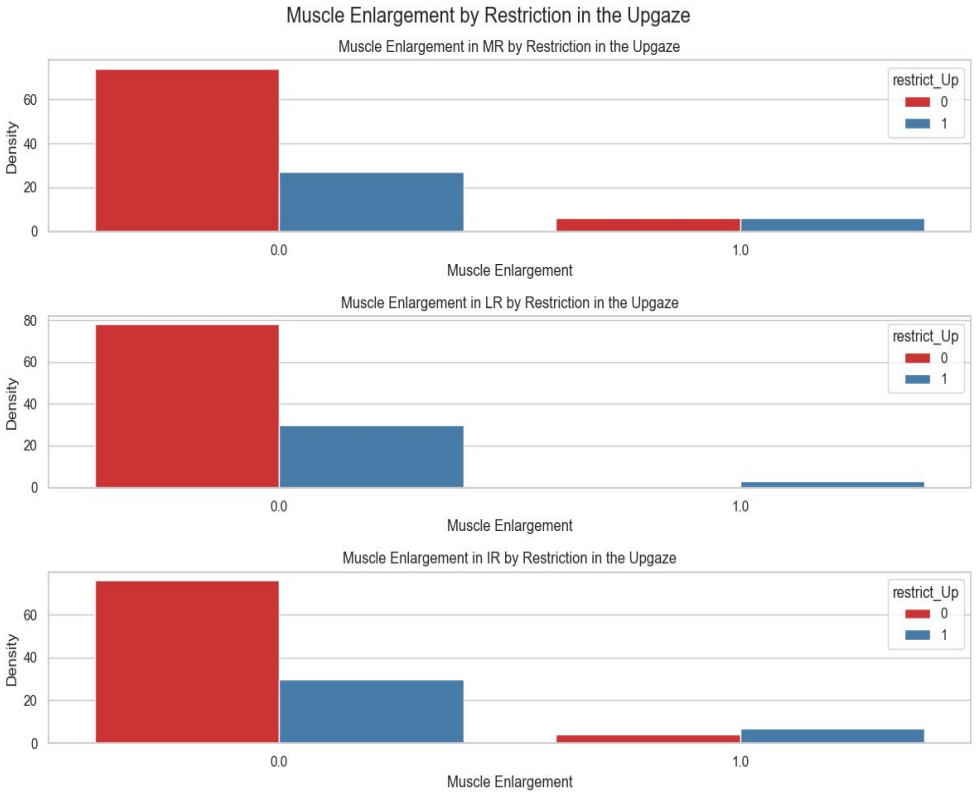
Chi-Square Test: Overall Restriction



Variable	p-value	Result
muscle_bi	0.0005737563440323	Reject the null hypothesis

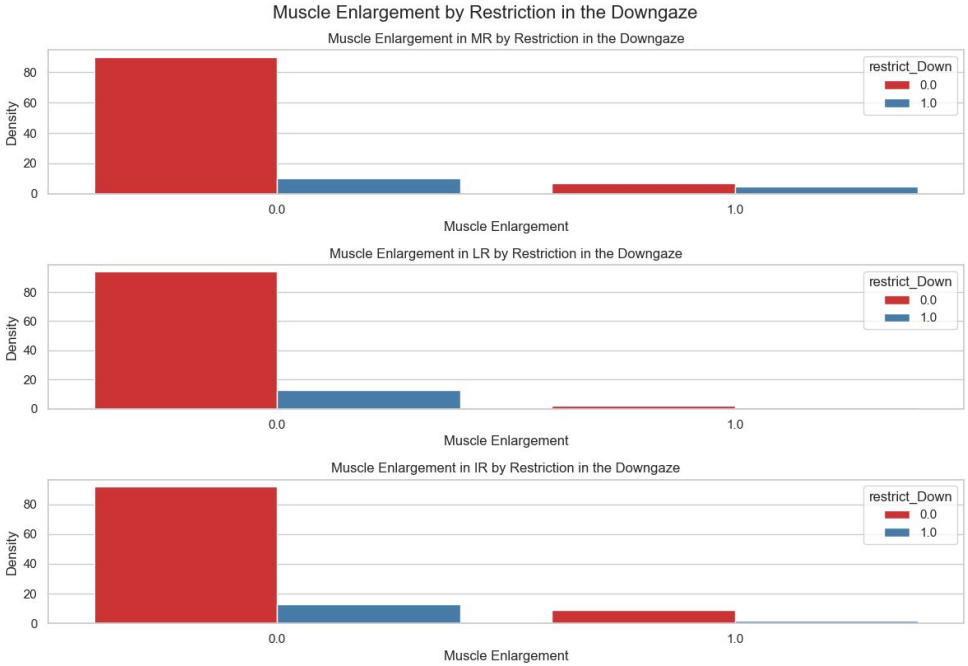
We found that patients with at least one enlarged muscle are much more likely to show motility restriction.This relationship is statistically significant, meaning it’s unlikely to be due to chance.

Fisher’s Exact Test: Restriction in the Upgaze



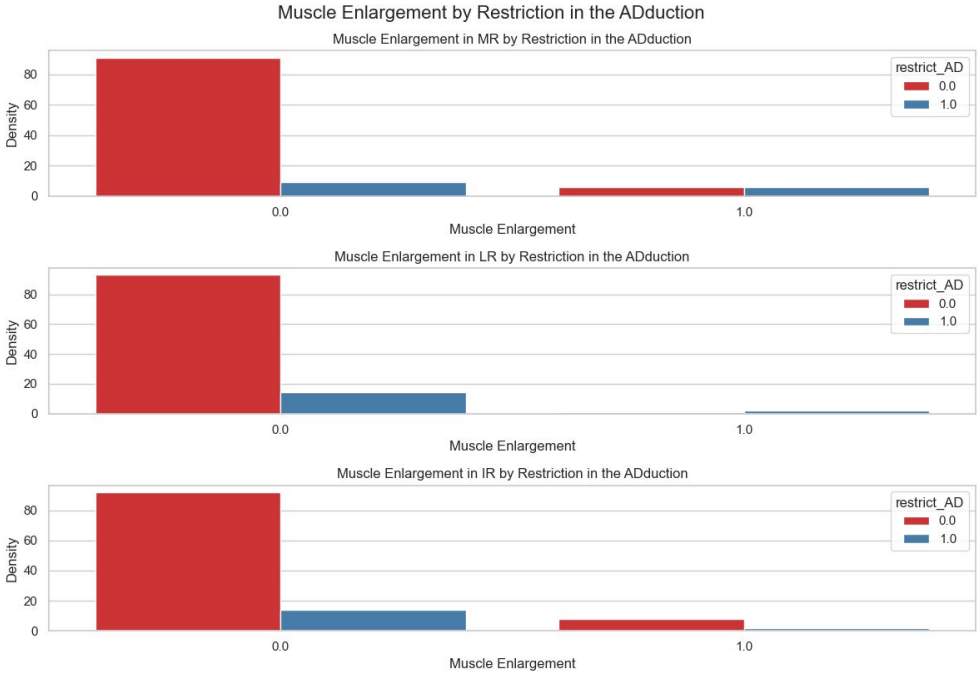
Muscle	p-value	Result
MR size	0.1054715165939738	Fail to reject the null hypothesis
LR size	0.0245970741383585	Fail to reject the null hypothesis
IR size	0.0349855259691564	Fail to reject the null hypothesis

Fisher’s Exact Test: Restriction in the Downgaze



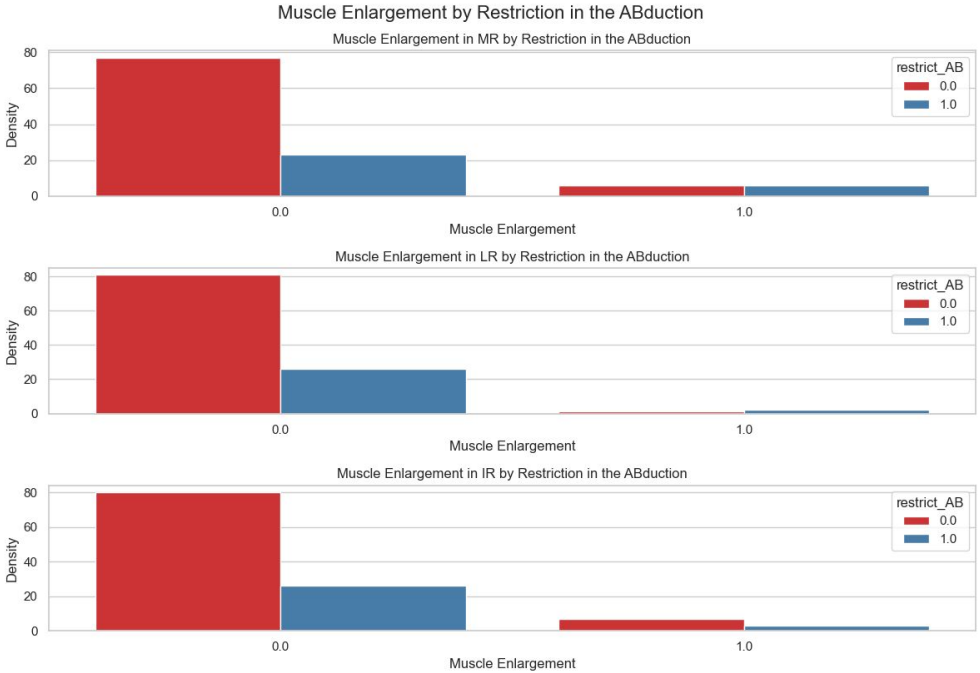
Muscle	**p-value**	**Result**
MR size	0.0099528573438809	Fail to reject the null hypothesis
LR size	0.3379668242053564	Fail to reject the null hypothesis
IR size	0.633377526638793	Fail to reject the null hypothesis

Fisher’s Exact Test: Restriction in the ADduction



Muscle	p-value	Result
MR size	**0.0012188538233949**	**Reject the null hypothesis**
LR size	0.0548605319247521	Fail to reject the null hypothesis
IR size	0.6268876598736229	Fail to reject the null hypothesis

Fisher’s Exact Test: Restriction in the ABduction



Muscle	p-value	Result
MR size	0.0747901367689634	Fail to reject the null hypothesis
LR size	0.1587989991659716	Fail to reject the null hypothesis
IR size	0.7091664080101487	Fail to reject the null hypothesis

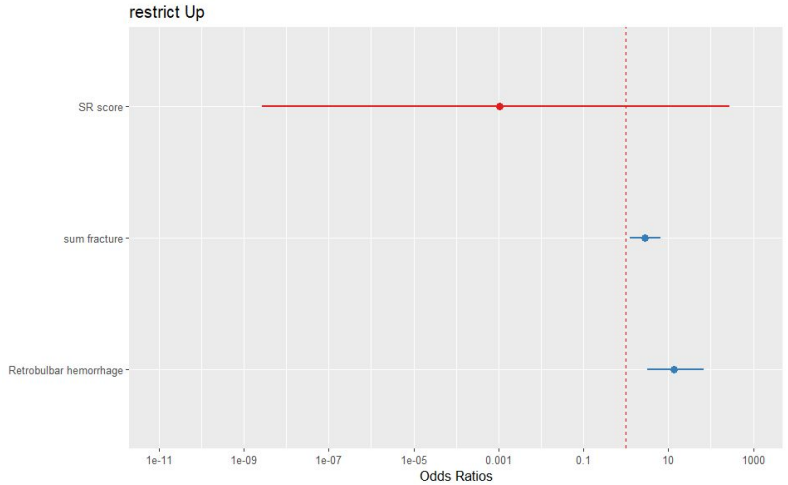
Logistic Regression

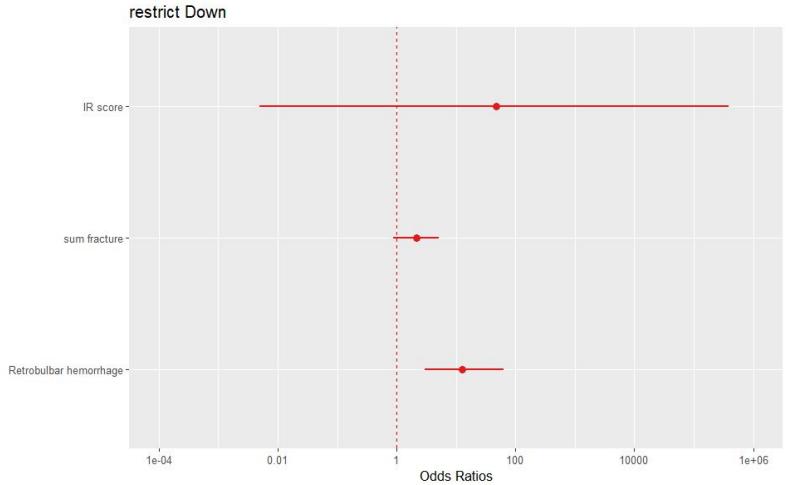
- Fit logistic regression models split by gaze restriction type
  - Upgaze, Downgaze, Adduction, Abduction, Any

- Initial predictors from hypothesized schematic: Retrobulbar_hemorrhage, SR, IR, MR, LR, sum_fracture
  - SR, IR, MR, LR scores are calculated from subtracting the control eye size from the fractured eye size to create a difference score

- Other predictors did not seem to significantly affect the model

Logistic Regression: Upgaze and Downgaze

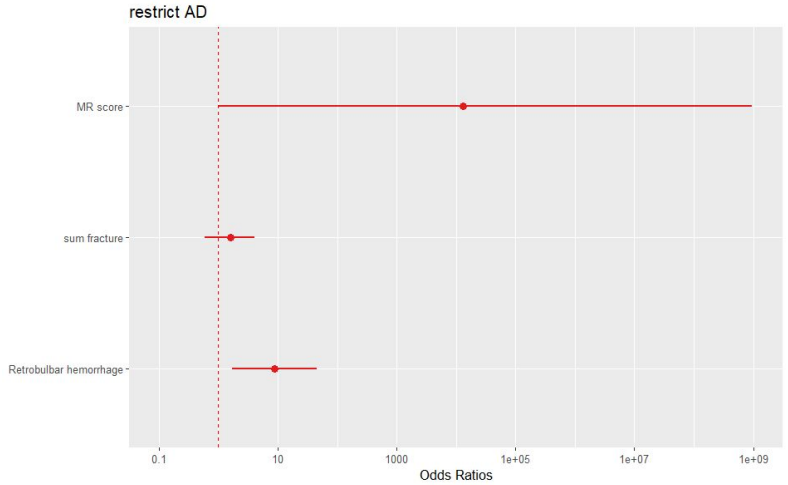


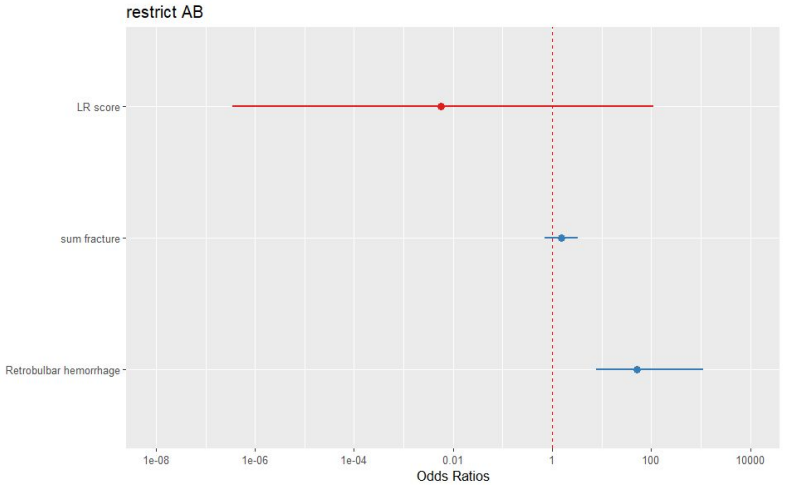


Coefficient	Estimate	SE	Pr(>|z|)
(Intercept)	-3.7	0.86	>0.0001***
SR_score	-6.86	6.3	0.28
sum_frac	1.012	0.42	0.02*
Ret_hem	2.6	0.77	0.0007***

Coefficient	Estimate	SE	Pr(>|z|)
(Intercept)	-3.6	0.93	0.0001***
IR_score	3.85	4.5	0.4
sum_frac	0.75	0.44	0.08.
Ret_hem	2.53	0.77	0.0009***

Logistic Regression: Adduction & Abduction

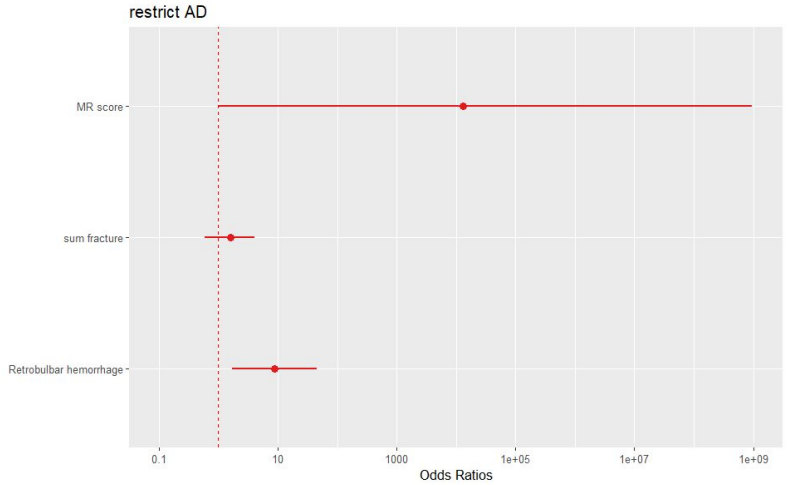




Coefficient	Estimate	SE	Pr(>|z|)
(Intercept)	-3.6	0.96	0.0002***
MR_score	9.48	5.23	0.07
sum_frac	0.47	0.47	0.32
Ret_hem	2.16	0.82	0.009**

Coefficient	Estimate	SE	Pr(>|z|)
(Intercept)	-2.12	0.7	0.002**
LR_score	-5.17	4.86	0.29
sum_frac	0.45	0.39	0.25
Ret_hem	3.93	1.17	0.0008***

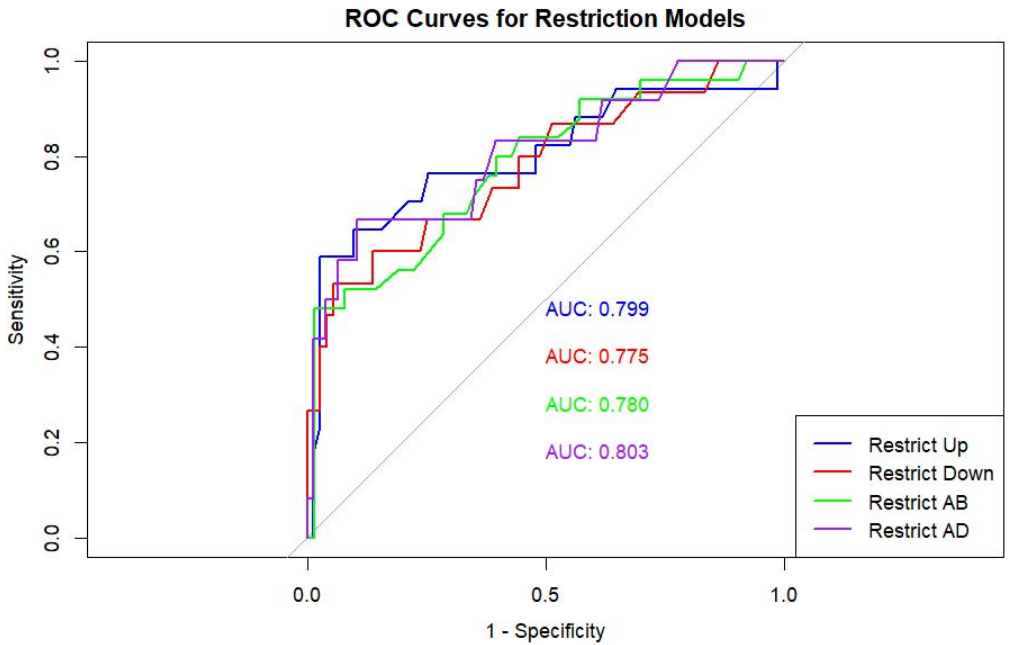
Logistic Regression: ADduction Interpretation (Non Log Terms)



Coefficient	Estimate	2.5%	97.5%
(Intercept)	0.03	0.003	0.16
MR_score	1.3e+04	1.01	9.6e+08
sum_frac	1.61	0.59	4.07
Ret_hem	8.66	1.68	45.29

- The point estimates as well as the 95% confidence interval have been translated to non log terms and are now interpretable
- A patient with retrobulbar hemorrhage has **8.66** times higher odds of AD restriction compared to a patient without a hemorrhage
- We can be 95% confident that this true odds ratio lies between **1.68 and 45.29**, and this interval is s**tatistically significant** as it doesn't contain 1 (which would be exactly equal odds of restriction with or without a hemorrhage)
- This means that Retrobulbar Hemorrhage significantly impacts the outcome of AD restriction.
- In addition, MR_score has a big standard error, which might be due a low frequency of enlarged MR muscles (only 12 out of 123 patients had an enlarged MR muscle).

Logistic Regression: ROC/AUC



- All four models perform well
- Retrobulbar_hemorrhage is a consistently good predictor
- Sum_fracture also seems to perform well
- Enlargement does not consistently predict restriction
- Next steps: try to account for variation due to individuals

Logistic Regression with Random Intercepts: Paired Enlarged Muscle and Restriction

glmer(restrict_AD ~ MR_size + (1|Patient_ID), data = cvf_split, family = “binomial”)
Fixed Effects:

	Estimate	Standard Error	Z-Value	Pr(>|z|)
(Intercept)	-2.8332	0.2854	-9.927	< 2e-16 ***
MR_size	2.8332	0.6440	4.399	1.09e-05 ***

glmer(restrict_AB ~ LR_size + (1|Patient_ID), data = cvf_split, family = “binomial”)
Fixed Effects:

	Estimate	Standard Error	Z-Value	Pr(>|z|)
(Intercept)	-1.960	0.195	-10.051	< 2e-16 ***
LR_size	2.653	1.240	2.139	0.0324 *

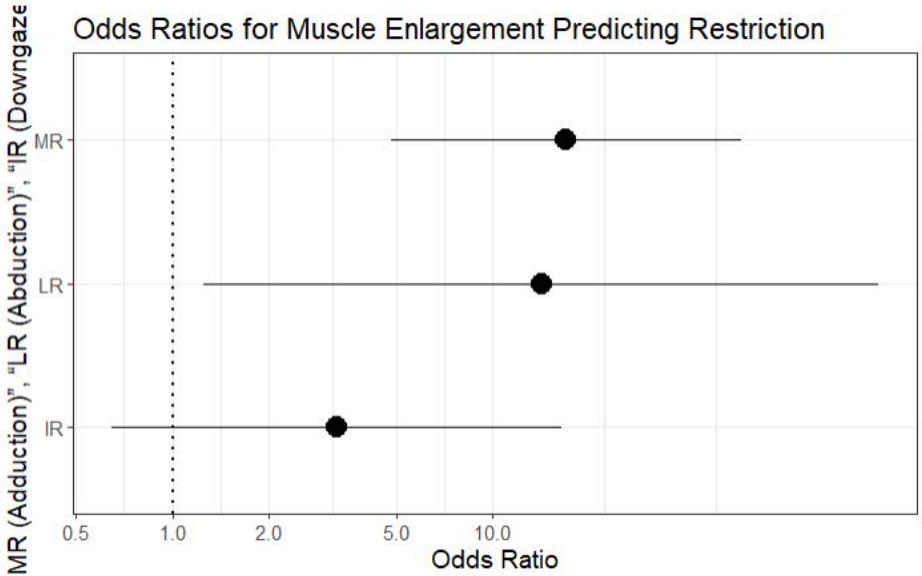
No test for SR since no patient had an enlarged superior rectus muscle

glmer(restrict_Down ~ IR_size + (1|Patient_ID), data = cvf_split, family = “binomial”)
Fixed Effects:

	Estimate	Standard Error	Z-Value	Pr(>|z|)
(Intercept)	-2.6856	0.2669	-10.06	< 2e-16 ***
IR_size	1.1815	0.8269	1.43	0.153

Odds Ratios and Plots for Muscle Restriction

Model	Odds Ratio	95% CI (Lower–Upper)
MR	17.0	(4.81, 60.07)
LR	14.2	(1.25, 161.42)
IR	3.26	(0.65, 16.45)



Logistic Regression with Random Intercepts: Paired Enlarged Muscle and Restriction (Opposite direction)

glmer(restrict_AB ~ MR_size + (1|Patient_ID), data = cvf_split, family = "binomial")

Predictor	Estimate	Std. Error	z value	p-value
(Intercept)	-2.0794	0.2080	-9.997	< 2e-16 ***
MR_size	2.0794	0.6137	3.388	0.000703 ***

No test for SR since no patient had an enlarged superior rectus muscle

glmer(restrict_AD ~ LR_size + (1|Patient_ID), data = cvf_split, family = "binomial")

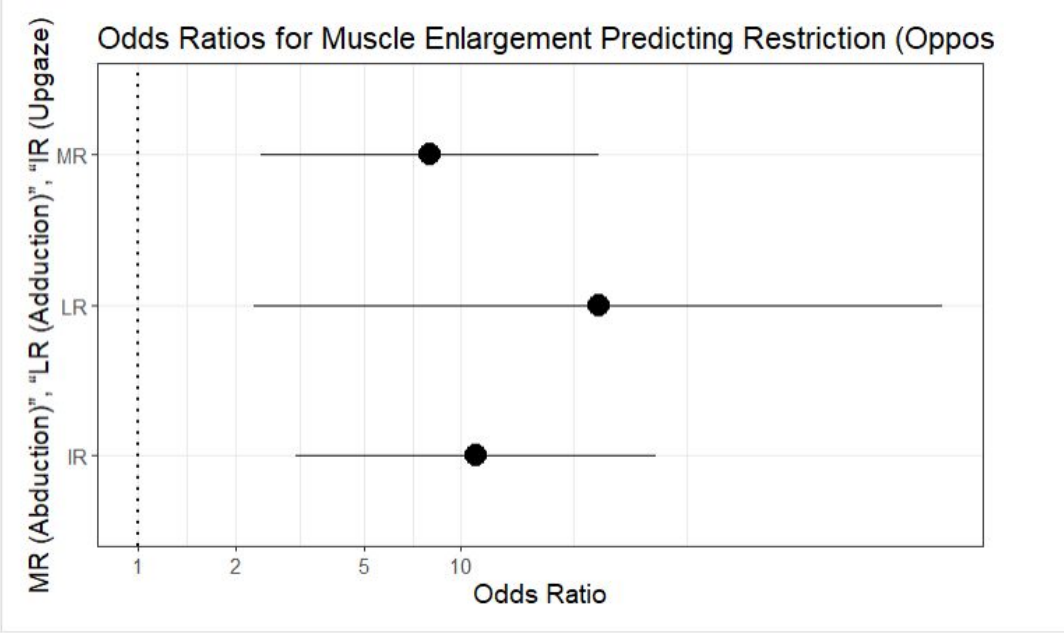
Predictor	Estimate	Std. Error	z value	p-value
(Intercept)	-2.5873	0.2515	-10.288	< 2e-16 ***
LR_size	3.2805	1.2503	2.624	0.0087 **

glmer(restrict_Up ~ IR_size + (1|Patient_ID), data = cvf_split, family = "binomial")

Predictor	Estimate	Std. Error	z value	p-value
(Intercept)	-1.8475	0.1902	-9.713	< 2e-16 ***
IR_size	2.4071	0.6550	3.675	0.000238 ***

Odds Ratio and Plots for Opposite Muscle Restriction

Model	Odds Ratio	95% CI (Lower–Upper)
MR	8.00	(2.40, 26.64)
LR	26.59	(2.29, 308.29)
IR	11.10	(3.07, 40.08)



Logistic Regression with Random Intercepts: Enlargement & Other Conditions

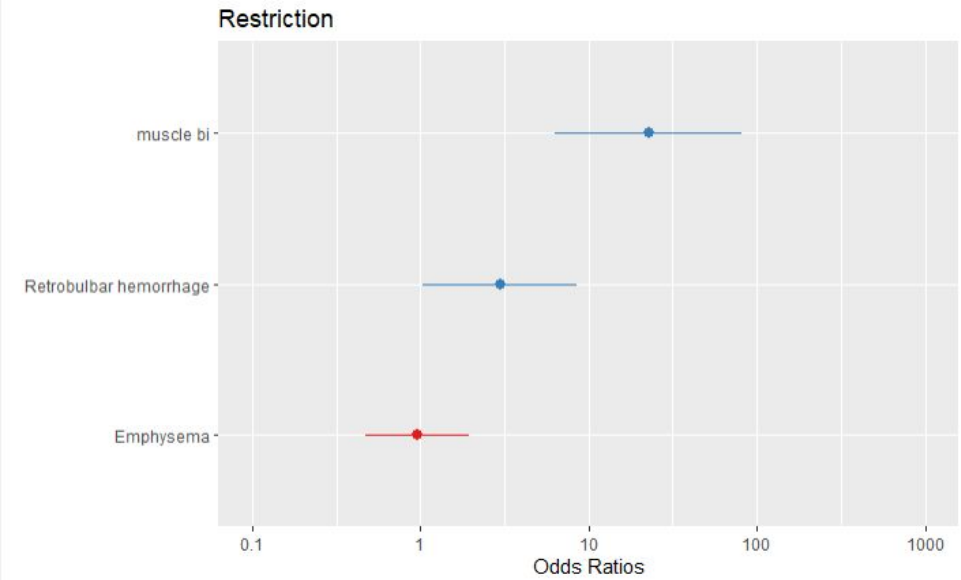
glmer(Restriction ~ muscle_bi + Retrobulbar_hemorrhage + Emphysema + (1|Patient_ID), data = cvf_split, family = “binomial”)

Fixed Effects:

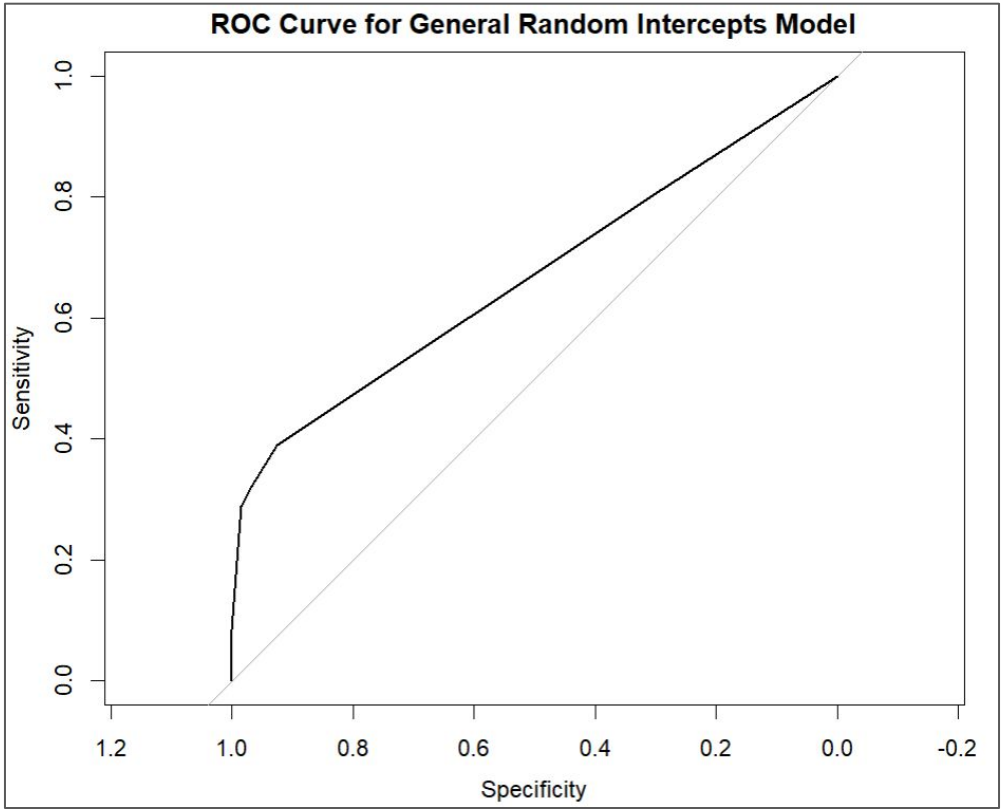
	Estimate	Standard Error	Z-Value	Pr(>|z|)
(Intercept)	-1.56514	0.21345	-7.333	2.26e-13 ***
muscle_bi	3.12055	0.65505	4.764	1.90e-06 ***
Retrobulbar_ hemorrhage	1.08456	0.53440	2.029	0.0424 *
Emphysema	-0.05307	0.36219	-0.147	0.8835

Odd Ratios and Plots

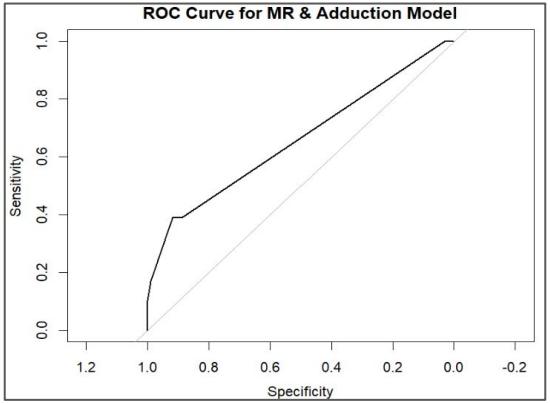
Predictor	Odds Ratio	95% CI (Lower–Upper)
(Intercept)	0.21	0.14 – 0.32
muscle_bi	22.66	6.28 – 81.82
Retrobulbar hemorrhage	2.96	1.04 – 8.43
Emphysema	0.95	0.47 – 1.93

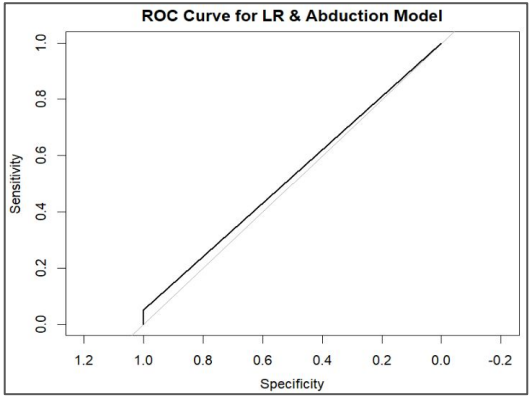


ROC Curve for Enlargement & Other Conditions Model

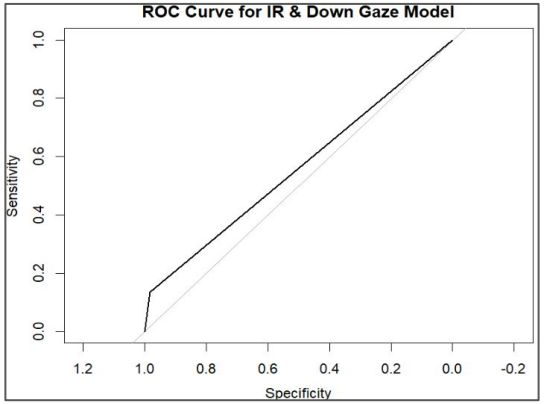


ROC Curves for Paired Muscle and Restriction Models

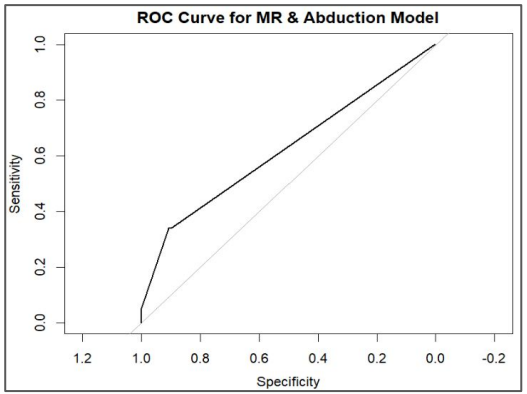


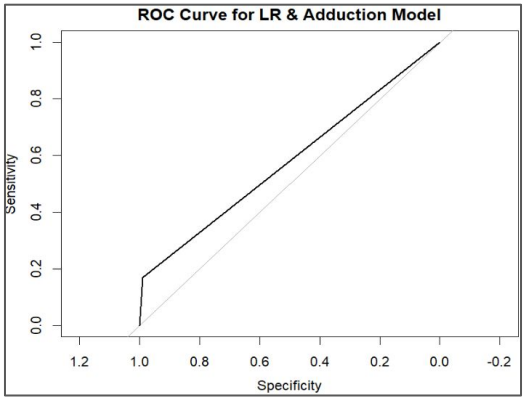


No ROC Curve for SR Muscle Pairing

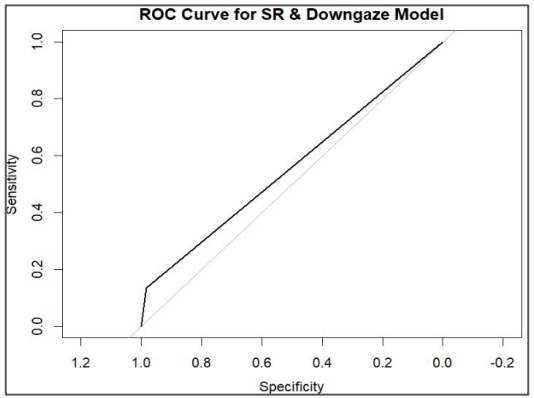


ROC Curves for Opposite Muscle and Restriction





No ROC Curve for SR Muscle Pairing



Conclusion

- **Key Findings:**
  - The **absolute increase in muscle surface area values** alone **did not consistently predict restriction** in classical hypothesis tests.
  - Model-based methods (e.g., logistic regression) highlighted **Retrobulbar hemorrhage** as a robust predictor.
  - The **binary variable muscle_bi** (patients with at least one enlarged muscle) however was **significantly associated with restriction**.
  - When broken down by individual muscles:
    - MR_size (enlarged medial rectus) was significantly associated with:
      - Restriction in ADduction
    - IR_size showed no consistent significant associations.
    - LR_size showed no consistent significant associations, likely due to its low occurrence (only 3 patients)
    - SR_size could not be tested because no patients had superior rectus enlargement (SR_size = 0 across all cases).
  - Logistic regression with random intercepts showed significant associations between specific muscle enlargement and restriction direction.
  - When any muscle was enlarged, the odds of restriction increased more than 22 times, suggesting the clinical importance of muscle enlargement when present.
  - Emphysema was not a significant predictor in our patient-adjusted models; clinicians should prioritize their attention to patients with retrobulbar hemorrhage + muscle enlargement.