The GAINS trial - Growth and Anabolism In Intensive care Survivors

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Abstract

Background

To explore the feasibility, safety and potential benefits from administration of nandrolone to patients in the recovery phase from critical illness weakness.

Methods

In this phase 2 randomized controlled trial, adult critically ill patients admitted for longer than 7 days with significant weakness, received nandrolone ((males 200 mg, females 100 mg) or placebo weekly, up to a total of three doses. Primary outcome measures were improvement in grip strength, medical research council (MRC) muscle strength sum score, and functional activity level (Chelsea critical care assessment tool (CPAx)).

Results

22 patients were enrolled between September 2017 and May 2019. No significant adverse events were detected. Median grip strength change was non-significantly greater in the nandrolone group (left hand (9.9 vs 4.4, p = 0.190), right (5.8 vs 3.0, p = 0.343)). The discharge CPAx and ICU mobility scores scores were higher in the nandrolone group, although there was no difference in the change in CPAx score (16.4 vs 17.2, p = 0.865). There were no changes in ultrasound detected muscle thickness between groups.

Conclusions

In patients with prolonged critical illness, nandrolone appears to be safe but a larger study, potentially combined with resistance exercise, is needed to definitively address the potential benefits.

Trial registration: ANZCTR registration number : ACTRN12616000835448. Registered 27/6/2016.

https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=370920

Introduction

Intensive Care Unit (ICU) acquired weakness, the result of catabolism, immobility and critical illness polymyoneuropathy, is of significant consequence to long-stay ICU patients. [1] Despite recent advances in prevention through rehabilitation and nutrition, it is estimated that one-quarter to one-half of long-stay ICU survivors live with significant weakness as a consequence of their illness, resulting in impaired mobility and function.[2, 3] The loss of lean body mass in critical illness is related to prolonged catabolism, immobility and critical illness polymyoneuropathy, but is also associated with misalignment between catabolic and anabolic hormones.[4–6] Testosterone levels in critically ill patients are extremely low, even in the recovery phase from acute illness. [7, 8]One potential treatment may be to provide anabolic support in the recovery phase from prolonged critical illness. [9]

Anabolic steroids stimulate protein and muscle synthesis. Many synthetic anabolic steroids have had modifications to the testosterone structure to maximise anabolic properties, whilst attempting to eliminate the androgenic effects. Nandrolone or oxandrolone exhibit significantly greater selectivity for myotropic properties, with minimal androgenic effects.[10] potentially minimising any adverse outcomes.

Nandrolone has previously been used successfully (compared with testosterone or placebo) in a randomized controlled trial to reverse weight loss in human immunodeficiency virus/acquired immunodeficiency sydnrome (HIV/AIDS) patients. [7–9] It has also been used in patients with chronic obstructive pulmonary disease (COPD) to improve respiratory function and muscle wasting.[10] Testosterone and oxandrolone have been shown to have beneficial effects on muscle catabolism in patients with burns.[11] Small previous studies have suggested nandrolone to be beneficial for patients recovering from critical illness. [12, 13]

We designed a phase II randomised controlled trial to explore the feasibility, safety and potential benefits on muscle strength and recovery from critical illness from nandrolone, or placebo. The primary objective of this trial was to assess whether nandrolone can improve muscle strength and functional recovery in deconditioned ICU patients.

Methods

Trial design

This investigator initiated study was a placebo controlled, randomised clinical trial conducted in two adult tertiary level ICUs in Perth Western Australia between September 2017 and May 2019. The study was approved by the Sir Charles Gairdner and Osborne Park Hospital HREC: RGS0000001841. Prospective registration of the trial was made on Australian and New Zealand Clinical Trials Registry (ACTRN12616000835448) and a clinical trials notification to the Therapeutic Goods Administration of the Australian Department of Health was made (CT-2016-CTN-02891)

Patients

Adult patients were eligible to participate if they had been admitted to the ICU for more than seven days, and had significant weakness as deemed by the treating clinician or weight loss (weight loss defined as body mass index (BMI) < 20 or greater than 10% weight loss in the last 6 months) as a result of the ICU stay or pre-ICU condition. Patients needed to be able to interact with physiotherapy, and to be receiving nutrition at estimated goal rate for at least 3 days prior to enrolment. Key exclusion criteria included inability to consent, intercurrent septic shock (defined as infection requiring vasopressor support), prostate or breast cancer, active cardiac disease (myocardial infarction in last two weeks or ejection fraction < 35%), ongoing non-curable reason for catabolic state (such as active malignancy, HIV with opportunistic infection or inadequate nutritional intake), normal baseline level of serum testosterone, pregnancy, nephrotic syndrome (proteinuria > 3 g/day) or elevated liver function tests (alanine aminotransferase > 5x normal) and impaired bilirubin excretion.

Randomisation and Blinding

Participants were randomised in a 1:1 ratio to receive nandrolone or placebo using a computer-generated randomisation list. The randomisation list was generated by an independent statistician, stratified by site and provided directly to the pharmacist responsible for preparing the study drug. The clinical teams, research staff and patients were masked to treatment allocation. To ensure blinding at administration, both the placebo (sterile water) and study drug were prepared in masked syringes (covered in aluminium foil) so that the contents were not visible to the person administering them.

Study Treatment

Intramuscular doses of nandrolone or placebo were administered into the lateral thigh, delivered weekly, up to a total of 3 doses. Female participants received 100 mg and males 200 mg. The dose selection was based on our own previous experience, as well as published data from other patient populations, and duration based on the likelihood of the patients still remaining in hospital for ongoing administration and measurements.[11–13] The first dose was administered while the patient was still in the ICU, but subsequent doses could be given when the patient had gone to the ward. The study drug was only administered if the patient was still in hospital, and thus not all patients received 3 doses.

Standard clinical management

No other changes to standard clinical management of these patients occurred. Improvements in critical illness weakness may also result from changes in physical therapy or nutrition. Estimates of daily caloric and protein intake were recorded by dietitians using food intake records, as well as duration of physical therapy received. The ICUs involved have dedicated physiotherapists and early rehabilitation is encouraged.

Outcome Measures

The primary outcome measures were an improvement in strength measures. The measures chosen were grip strength, measured by hand dynamometry, medical research council (MRC) muscle strength sum score, and functional activity level using the Chelsea critical care assessment tool (CPAx).[14] Hand dynamometry, MRC and CPAx scores were all measured by trained physiotherapists. Secondary outcome measures were change in body weight, mid arm circumference, ultrasound measured quadriceps muscle thickness, ICU length of stay (LOS) and hospital LOS.. Ultrasound measurements were taken by two trained clinicians, using previously described protocols.[15] All measures were taken at baseline and then weekly until discharge. MRC and CPAx were measured up to hospital discharge whereas the ICU mobility scale was measured until ICU discharge. Blood tests were also taken to monitor testosterone levels, haemoglobin, cholesterol and liver function. A follow-up phone call at 3 months following discharge was planned to assess the patient's functional state using the SF-36 score.

Statistical Analysis

As a phase II pilot study, an a priori sample size calculation to detect a specific effect size difference was not undertaken. Descriptive statistics were based on frequency distributions for categorical data and means, standard deviations, medians, IQRs, and ranges for continuous data. Group comparisons were based on treatment groups. Univariate analysis include χ^2 and Fisher Exact tests, as appropriate, for categorical comparisons, and Mann-Whitney *U* tests and *t* tests for comparison of continuous outcomes. Ventilation and LOS durations were estimated using Kaplan-Meier survival probabilities, with Log-Rank tests used to test group differences. Linear mixed models incorporating random subject effects were used to examine group differences in nutritional, physical rehabilitation and hormonal measures at days 1, 7, 14 and 21. Results are summarised as predicted marginal means and corresponding 95% CI. Outcome variables were dichotomised according to accepted cutoffs (MRC score < 48 = ICU acquired weakness, CPAx score ≤ 18 (at risk of physical disability on discharge[16] and ICU mobility scale score of 8 (walking with one assist). Statistical analysis was conducted using Stata 16.0 (StataCorp LLC, College Station, Texas) and IBM SPSS version 26.0 (Armonk, NY). All hypothesis tests are 2-sided, and *P* values < 0.05 are considered statistically significant.

Results

A total of 22 patients were enrolled in the study (21 at Sir Charles Gairdner and 1 at Royal Perth Hospital), with 11 in each group (Figure 1). Patients had a mean (SD) age of 66 (11) years, were predominantly male (13/22) and had an initial mean APACHE III score of 39.5 (26.6). Baseline characteristics are outlined in Table 1. Patients received their first dose of nandrolone, on average at day 15 after ICU admission. Despite randomisation, there were some differences in the baseline mobility and strength characteristics between the two groups. While these may have occurred due to chance, Medical research sum score (40.5 vs 28.2, p= 0.001), Critical Care Physical Assessment tool score (24.7 vs 14.8, p=0.011), ICU mobility scale (5.1 vs 2.9, p=0.005) and grip strength (9.6 vs 3.4 on the right, p = 0.165)) were all higher in the nandrolone groups at baseline (Table 1 and supplementary table 1). A CPAx score ≤18 (at risk) has previously categorised patients at risk of physical disability on discharge, and in this cohort, there was no significant difference between the groups (p=0.67).[16] Table 2 outlines the treatments received in the rehabilitation period, with the placebo group receiving more calories, protein and physiotherapy input.

Primary outcome

Table 3 shows the improvement in strength in the two groups. MRC change (from baseline to end measurement) was significantly higher in the placebo group (17.6 vs 9.3, p=0.001). Median grip strength change was non-significantly greater in the nandrolone group, for the left hand (9.9 vs 4.4, p =0.190), and the right (5.8 vs 3.0, p = 0.343). The discharge CPAx score and the discharge ICU mobility scores were higher in the nandrolone group, although there was no significant difference in the change in CPAx score (16.4 vs 17.2, p=0.865).

Secondary outcomes

More patients were discharged home in the nandrolone group than the placebo group (6 vs 0). Length of ICU (23 vs 14 days) and hospital (36 vs 26 days) stay, and mechanical ventilation (377 vs 168 hours) were all shorter in the nandrolone group, but with no difference in hospital or 90 day survival in either group. Supplemental table 1 outlines the changes in ultrasound measured quadriceps thickness over time, weight and biceps diameter, with no significant changes over time in these measurements between groups.

SF-36 results were available for 16 patients at 3 months after enrolment. Table 4 outlines the results by domain. All but 3 patients (in the nandrolone group) were living independently prior to hospitalisation. There was a non-significant trend towards improved physical functioning (56.6 vs 40.7, p=0.32) and reduced limitations due to physical functioning (58.3 vs 17.9, p =0.076) and reduction in pain (77.6 vs 47.4, p=0.065) in the nandrolone group, but no changes in the other domains.

Safety

We did not detect any adverse effects from nandrolone on the blood parameters we monitored (renal, liver function and lipids) (supplemental table 1). We did not record any other pre-specified significant adverse events with regards to cardiac failure or virilisation.

Study drug administration

Table 2 outlines the number of doses of study drug received in the two groups. 7 of the patients in the nandrolone group received 2, whereas 7 of the placebo group received 3 doses. All patients received at least one dose.

Discussion

To our knowledge, this is the first non-burns ICU randomized controlled study to look at the use of anabolic steroids. It showed that the administration of nandrolone to ICU patients with ICU acquired weakness appears to be both safe and feasible. There were no consistent significant differences in the primary outcomes between the two groups. Although the MRC change was greater in the placebo groups, the other co-primary outcomes showed no difference.

The cohort of patients studied appears to be representative of those with ICU acquired weakness. They had significant weakness, with baseline grip strength readings consistent with accepted cut-offs for ICU acquired weakness and MRC scores well below 48.[17] In keeping with the biological plausibility of providing anabolic steroids, these patients were testosterone deficient. [8]

In the nandrolone group, more patients were discharged home from hospital, with higher discharge CPAx and MRC scores. SF-36 scores in pain and limitations due to physical functioning at 3 months were also higher in the nandrolone group. However, as secondary outcomes these findings can only be hypothesis generating and are not reflected by the other outcome measures. The increase in MRC (change) was actually greater in the placebo group and while grip strength change was greater in the nandrolone group,

it was not significant, and there was no significant improvement in MRC scores, mobility scores or ultrasound measurements in the patients who received nandrolone. This may reflect the fact that we did not incorporate resistance exercise into the rehabilitation program, potentially a required component of muscle hypertrophy.[18]

We had considered the use of ultrasound might have been able to detect more subtle changes in muscle size.[15, 19] The lack of change seen may be because the duration of observation was not long enough to detect changes in muscle size, or nandrolone did not accelerate muscle growth compared with placebo, or that changing fluid status in recovering patients affected the readings. Muscle wasting in the ICU occurs early (in the first 1–2 weeks), and a recent study showed no correlation between caloric or protein debt and muscle thickness over one week. [20]

In setting up the trial, we wanted to measure the traditional components of ICU recovery – nutrition and physical rehabilitation. Early rehabilitation and dietitian review is standard practice in the participating ICUs. Of note, the placebo group received more calories and protein replacement, as well as more physiotherapy time, making it harder to separate out the contribution of nandrolone alone to the patients' recovery. We hypothesise that since the placebo group had longer duration of mechanical ventilation, they also more likely had a longer duration of nasogastric enteral feeding, which makes it easier to achieve nutritional targets (especially in the recently extubated patients), and longer duration of physiotherapy as they were receiving ventilator weaning assistance.

There are several limitations that need to be addressed. First, despite randomisation, there appears to be a degree of mismatch in the underlying characteristics of the enrolled patients. At baseline, the placebo group (which ended up having longer duration of mechanical ventilation) had lower MRC, CPAx and ICU mobility scale scores. The differences in length of stay are likely to reflect these baseline differences rather than the nandrolone. Understanding why the randomisation process wasn't entirely successful might relate to the heterogeneity of patients with ICU acquired weakness and the sample size. Second, whilst two ICUs were involved, the patients were predominantly enrolled from one ICU. Third, as a pilot study, the study was not powered to detect differences between the groups but rather to test the feasibility of the protocol and establish pilot data to guide further studies. Finally, this study did not address whether the dosing schedule and dose chosen were optimal. We elected to provide up to 3 doses based on estimates of how long patients would remain in hospital. It may be that a more prolonged course of nandrolone would be more beneficial, as used by authors in different settings, and combined with resistance exercise to promote muscle growth.[12, 21] Indeed, a single dose of nandrolone has not been shown to attenuate muscle atrophy during disuse.[22] However, a longer duration trial would require coordination across departments and settings.

Conclusion

Addressing persistent catabolism and testosterone deficiency has been suggested as a potential treatment for ICU acquired weakness. [23] In patients with prolonged critical illness, nandrolone appears

to be safe but a larger study, potentially also with a longer duration of nandrolone administration, is needed to definitively address the potential benefits.

Declarations

Ethics approval and consent to participate: The study was approved by the Sir Charles Gairdner and Osborne Park Hospital HREC: RGS0000001841. All patients provided written consent to participate.

Consent for publication N/A

Availability of data and material: The datasets generated during and/or analysed during the current study are not publicly available due to ethics approval restrictions but are available from the corresponding author on reasonable request.

Competing interests: The authors have no competing interests to declare.

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Authors' contributions: MA: Conceptualization, Investigation, Methodology, Writing-original, Supervision BW: Conceptualization, Investigation, Methodology, Writing- Reviewing and Editing. EM : Data curation, Investigation. Writing- Reviewing and Editing, NT,BM,EO, AC: Investigation, Methodology, Writing- Reviewing and Editing. EF: Data curation, Investigation. Writing- Reviewing and Editing, AJ: Analysis, Methodology, Writing - Reviewing and Editing.

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Tables

Table 1. Baseline Characteristics of Study Participants by Treatment Group

Characteristics	Placebo (n = 11)	Nandrolone (n = 11)
Demographics		
Sex, n (%)		
Female	5 (45.5%)	4 (36.4%)
Age, years	62.7 (11.9)	69.7 (9.6)
Body mass index (BMI), kg/m^2	26.9 (5.9)	26.9 (7.4)
Body mass index (BMI), <18.5 kg/m^2	1 (9.1)	2 (18.2)
Body mass index (BMI), >30 kg/m^2	4 (36.4)	4 (36.4)
Residence prior to admission		
Own home	11 (100%)	8 (72.7)
Supports at home	0	3 (27.3)
APACHE III score	37.8 (14.7)	41.6 (37.8)
Duration of ICU admission prior to enrolment (days)	15.2 (7.6)	14.2 (9.5)
Indication for ICU admission		
Post general surgical	4 (36.4%)	4 (36.4)
Neurological	2 (18.2)	1 (9.1)
Respiratory	3 (27.3)	0
Cardiovascular	2 (18.2)	1 (9.1)
Post cardiac surgery	0	3 (27.3)
Renal failure	0	1 (9.1)
Toxicological	0	1 (9.1)
Testosterone level[#]	3.23 (3.8)	
Males	1 (0.74)	3 (1.30)
Females		0.5 (0.30)
Baseline physical scores (at enrolment)		
Mid arm circumference (cm)		
Right	27.6 (5.0)	27.2 (6.1)
Left	27.4 (4.4)	27.3 (5.8)

Medical research council (MRC) sum score	28.2 (14.5)	40.5 (8.2)*
Chelsea Critical Care Physical Assessment Tool (CPAx)	14.8 (7.5)	24.7 (8.9)
CPAx ≤18 (at risk)	6 (54.5)	4 (36.4)
ICU mobility scale (IMS)	2.7 (1.3)	5.1 (1.9)
IMS < 8^	10	9
Grip strength	2.9 (0.4, 7.3)	6.5 (2.8, 10.2)
Left	3.4 (0.3, 6.2)	9.6 (3.2, 12.0)
Right		

Data are expressed as mean (standard deviation), frequency (prevalence in %), or median (interquartile range (25^{th}-75^{th} percentile).

#Normal range males 10-35 nmol/L. Females < 2nmol/L.

^ ICU mobility scale of 8 or above = walking with one assist.

Table 2. Treatments received during rehabilitation period

	Placebo	Nandrolone	
Corticosteroid use ***n(%)***	3 (27.3)	1 (11.1)	0.590
Calorie intake (kJ) ***mean (SD)***	1857 (465)	1259 (349)	0.003
Protein intake (g/day) ***mean (SD)***	85.7 (20.8)	59.3 (18.9)	0.005
Duration of physiotherapy received (minutes) ***med (IQR)***	240 (173-500)	135 (85-240)	0.067
Number of doses received ***n***			0.062
1	2	2	
2	2	7	
3	7	2	

Table 3. Primary and Secondary Outcomes

Outcomes	Placebo	Nandrolone	*P* value
Primary outcomes			
MRC change*#	17.6 (8.9)	9.3 (5.7)	0.001
Grip strength change (L)	4.4 (0.8,7.0)	9.9 (4.9,12.1)	0.190
Grip strength change (R)	3.0 (2.1, 6.3)	5.8 (3.6, 8.0)	0.343
ICU mobility score change*	3 (2.0)	3.6 (2.1)	0.530
CPAx change	16.4 (11.1)	17.2(7.9)	0.865
Secondary outcomes			
Length of invasive ventilation, hours	377 (189-581)	168 (164-305)	0.076
ICU length of stay, days	23 (16–29)	14 (12–18)	0.047
Hospital length of stay, days	36 (28-43)	26 (20-37)	0.056
ICU readmission rate, n (%)	3 (30%)	1 (11.1%)	0.582
ICU survival, n (%)	9 (82%)	11 (100%)	0.476
90 day survival, n (%)	9 (82%)	11 (100%)	0.476
Discharge destination			0.010
Home	0 (0%)	6 (54%)	
Other (rehab/other hospital)	9 (82%)	5 (45%)	
Death in hospital	2 (18%)	0 (0%	
Discharge MRC score*	42.7 (13.4)	49.8 (7.6)	0.006
MRC ≥48	4 (36.4%)	6 (54.5%)	0.673
Discharge ICU mobility scale score*	5.8 (2.2)	8.4 (1.7)	0.005
IMS ≥8 (walking with one assist)	3 (27.3%)	6 (54.5%)	0.637
Discharge CPAx score*	31.6 (11.1)	42.8 (6.0)	0.011
CPAx > 18	7 (63.6%)	8 (72.7%)	0.471

*Data are expressed as median (interquartile range (25^{th}-75^{th} percentile, values separated by comma), *mean (std deviation) or frequency (prevalence in %).*

#Change relates to difference from baseline measurement at enrolment, to last measured score prior to discharge.

Table 4. SF 36 scores at 3 months following enrolment.

	Placebo (n=7)	Nandrolone (n=9)	p-value
Physical functioning	40.7 (28.4)	56.6 (32.6)	0.32
Role limitations due to physical functioning	17.9 (27.8)	58.3 (50)	0.076
Role limitations due to emotional functioning	42.9 (53.5)	74.1 (43.4)	0.22
Energy/fatigue	40 (31.8)	48.9 (24.8)	0.54
Emotional well-being	76 (22.9)	80.1 (30.9)	0.73
Social functioning	59.1 (31.9)	72.3 (31.1)	0.42
Pain	47.4 (27.4)	77.6 (31.6)	0.065
General health	50 (27.2)	51.7 (29.4)	0.91
Health change	46.4 (33.6)	41.7 (33.1)	0.78

Values displayed as mean (standard deviation).

Supplemental table 1. Changes in physical strength and laboratory values over time.

	Baseline	Day 7	Day 14	Day 21
Grip strength (kg/force) (R)				
Placebo	3.6 (0.7,6.5)	7.4 (4.4, 10.4)	7.7 (3.7,10.7)	7.7 (4.5,11.0)
Nandrolone	8.4 (5.5, 11.3)	10.3 (7.3,13.2)	11.9 (8.5, 15.4)	13.3 (9.9, 16.7)
Grip strength (L)				
Placebo	4.1 (0.5, 7.7)	5.7 (2.0, 9.4)	7.6 (3.9, 11.3)	8.3 (4.5, 12.1)
Nandrolone	8.5 (4.9, 12.1)	11.5 (7.8, 15.2)	12.2 (8.0, 16.3)	16.5 (12.5, 20.7)
Weight (kg)				
Placebo	78.1 (63.8, 92.3)	76.5 (62.2, 90.7)	72.8 (58.4, 87.2)	*
Nandrolone	74.1 (61.3, 86.9)	71.6 (58.5, 84.6)	71.2 (57.0, 85.5)	
Mid-Quad USS (R)				
Placebo	1.13 (0.9, 1.4)	1.06 (0.8, 1.3)	1.09 (0.8, 1.4)	*
Nandrolone	1.32 (1.1, 1.6)	1.29 (1.0, 1.6)	1.11 (0.8, 1.5)	
Mid-Quad USS (L)				
Placebo	1.23 (1.0, 1.5)	0.99 (0.7, 1.2)	1.12 (0.8, 1.4)	*
Nandrolone	1.27 (1.0, 1.5)	1.24 (1.0, 1.5)	1.17 (0.9, 1.5)	
2/3 Quad USS (R)				
Placebo	0.95 (0.7, 1.2)	0.83 (0.6, 1.1)	0.94 (0.7, 1.2)	*
Nandrolone	1.07 (0.8, 1.3)	1.10 (0.9, 1.3)	0.84 (0.6, 1.1)	
2/3 Quad USS (L)				
Placebo	1.02 (0.8, 1.2)	0.83 (0.6, 1.0)	0.97 (0.7, 1.2)	*
Nandrolone	0.99 (0.8, 1.2)	1.01 (0.8, 1.2)	1.03 (0.8, 1.3)	
Biceps (cm) (L)				
Placebo	28.8 (25.2, 32.4)	28.8 (25.2, 32.4)	26.3 (22.4, 30.3)	*
Nandrolone	27.8 (24.7, 30.8)	26.6 (23.3, 29.8)	26.5 (22.7, 30.3)	
Biceps (cm) (R)				*
Placebo	29.5 (25.9, 33.0)			

Nandrolone	28.1 (25.1, 31.1)	28.9 (25.4, 32.5)	26.3 (22.5, 30.1)	
		26.2 (23.0, 29.3)	26.2 (22.6, 29.7)	
Blood parameters				
Haemoglobin				
Placebo	94.2 (85.9, 102)	95.3 (86.8, 104)	95.3 (86.8, 104)	90.4 (81.7, 99.1)
Nandrolone	84.7 (76.5, 93)	91.2 (82.9, 99.5)	91.2 (82.9, 99.5)	95.7 (86.8, 105)
ALT				
Placebo	115.4 (82.0, 149)	55.8 (20.4, 91.3)	30.1 (-7.9, 68.0)	39.5 (-1.8, 80.7)
Nandrolone	55.9 (22.7, 89.2)	41.9 (8.5, 75.3)	34.4 (-3.7, 72.5)	28.0 (-35.3, 91.
Triglycerides				
Placebo	2.2 (1.3, 3.2)	2.2 (1.2, 3.2)	2.5 (1.5, 3.4)	2.2 (1.2, 3.2)
Nandrolone	2.0 (1.1, 2.9)	2.3 (1.4, 3.2)	2.3 (1.3, 3.3)	1.9 (0.9, 2.9)
LDL				
Placebo	2.5 (1.8, 3.3)	2.5 (1.7, 3.3)	2.7 (2.0, 3.5)	2.8 (2.0, 3.6)
Nandrolone	1.4 (0.7, 2.1)	1.8 (1.1, 2.5)	1.3 (2.0, 3.6)	1.6 (0.7, 2.4)
Albumin				
Placebo	30.8 (27.9, 33.8)	30.0 (26.9, 33.2)	31.1 (27.8, 34.4)	31.8 (27.9, 35.7)
Nandrolone	30.1 (27.1, 33.1)	32.2 (29.1, 35.3)	30.4 (27.0, 33.9)	32.8 (27.9, 37.8)
Creatinine				
Placebo	80.3 (36.5, 124)	87.1 (41.7,132)	61.4 (14.3, 108)	52.4 (-2.0, 106.9)
Nandrolone	175 (131.2, 218.7)	166.4 (123, 210)	139 (91.9, 186)	102.5 (30.5, 175)

ALT – alanine aminotransferase, LDL – low density lipoprotein

All values are estimated mean, (95% confidence interval).

Ultrasound measurements are in cm.

* Insufficient data points for inclusion in table.

Figures

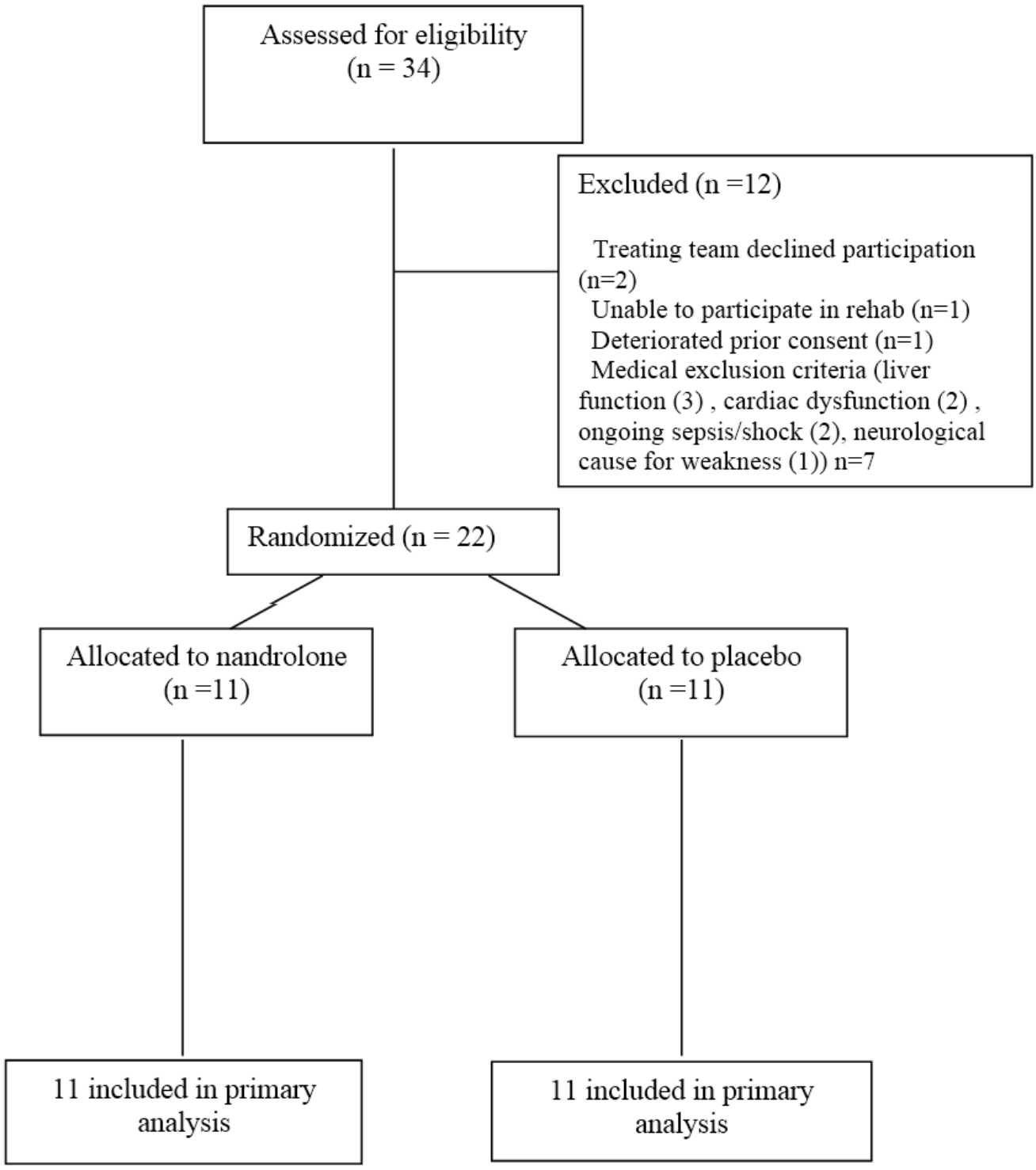

Figure 1

Analysis, Flow chart

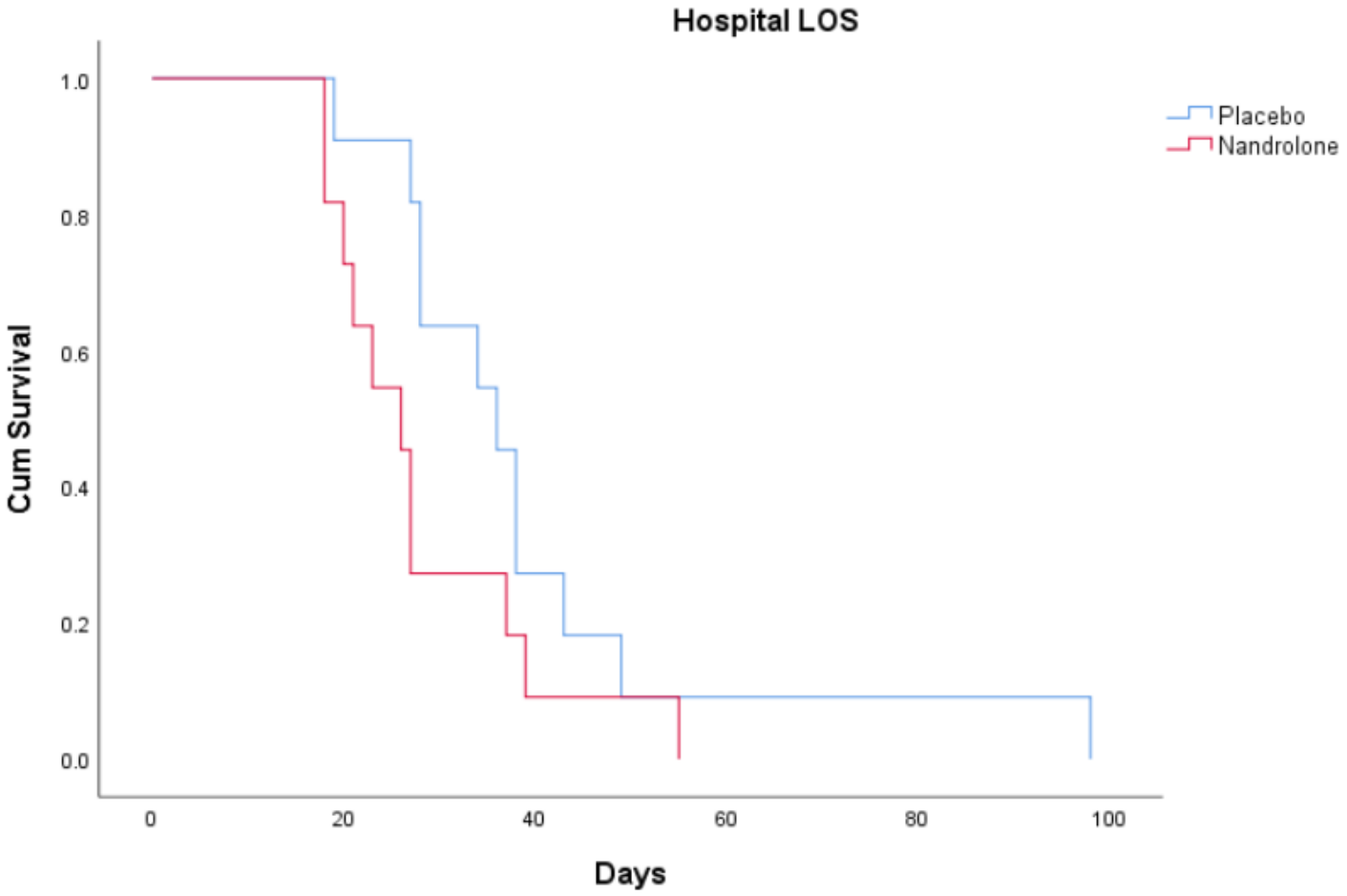

Figure 2

Kaplan Meier Curve for hospital length of stay.