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Hypnosis versus Placebo during Atrial Flutter Ablation: the PAINLESS Study.

A randomized controlled trial

Brief head: Hypnosis during atrial flutter ablation

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STRUCTURED ABSTRACT

Objective: We aimed to assess the superiority of hypnosis versus placebo on pain perception and morphine consumption during typical atrial flutter (AFI) ablation.

Background: AFI ablation commonly requires intravenous opioid for analgesia, which can be associated with adverse outcomes. Hypnosis is an alternative technique with rising interest but robust data in electrophysiology procedures are lacking.

Methods: We conducted a single-centre, randomized controlled trial to compare hypnosis and placebo during AFI ablation. In addition to the randomized intervention, all patients were treated according to our institution's standard of care analgesia protocol (administration of 1mg of intravenous morphine in case of self-reported pain ≥ 5 on a 11-point numeric rating scale, or on demand). The primary endpoint was perceived pain quantified by patients using a visual analog scale.

Results: Between October 2017 and September 2019, 113 patients (age 70 ± 12 years, 21% females) were randomized to hypnosis (n=56) or placebo (n=57). Mean pain score was 4.0 ± 2.2 in the hypnosis group versus 5.5 ± 1.8 in the placebo group ($P < 0.001$). Pain perception, assessed every 5 minutes during the whole procedure, was consistently lower in the hypnosis group. Patients' sedation score was also better in the hypnosis group than in the placebo group (8.3 ± 2.2 vs 5.4 ± 2.5 ; $P < 0.001$). Finally, morphine requirements were significantly lower in the hypnosis group (1.3 ± 1.3 mg) compared to the placebo group (3.6 ± 1.8 mg; $P < 0.001$).

Conclusion: In this first randomized trial, hypnosis during AFI ablation was superior to placebo for alleviating pain and reducing morphine consumption.

KEY WORDS: Hypnotic therapy; Randomized trial; Atrial flutter; Pain; Quality of care; Morphine

CONDENSED ABSTRACT

This randomized study assessed the superiority of hypnosis (56 patients) versus placebo (57 patients) regarding pain perception and opioid consumption during typical atrial flutter ablation. Pain perception, measured by a validated visual analog scale was significantly lower in the hypnosis group (4.0 ± 2.2 points vs 5.5 ± 1.8 4; $P < 0.001$), and this effect was maintained throughout the procedure. Morphine consumption was significantly lower in the hypnosis group than in the placebo group (1.3 ± 1.3 mg vs 3.6 ± 1.8 mg respectively, $P < 0,001$). Hypnosis reduces pain perception and morphine consumption, which may lead to less opioid-related complications.

ABBREVIATION LIST:

AFI: Atrial flutter

NRS: numeric rating scale

VAS: visual analog scale

INTRODUCTION

Catheter ablation for cavotricuspid isthmus dependent atrial flutter (AFI) is a common technique with more than 18 000 procedures performed per year in France (1–5). Pain during ablation must be efficiently controlled for procedural efficiency and success.

AFI ablations are typically performed under conscious sedation using opioids such as morphine and/or benzodiazepines such as Diazepam or Midazolam (6). Opiate use is associated with a risk of respiratory depression, hypotension and, in rare circumstances, mortality (7–9). Alternatives to opioid administration, such as hypnosis, have been successfully used to relieve pain during invasive procedures (10). Hypnosedation uses hypnosis combined with locoregional anesthesia and small doses of intravenous analgesic. It has recently been reported to be more efficacious than conventional analgesia during electrophysiology procedures in case reports, case series and prospective non-randomized studies (11–13).

This prospective, randomized study aimed to compare pain perception and morphine consumption in patients receiving hypnosis versus placebo during AFI ablation.

METHODS

Study Setting and Population

The PAINLESS trial (Clinical Trial number NCT03250871) was conducted between October 2017 and September 2019 at the Cardiology Department of the University Hospital of Poitiers, France. All consecutive patients ≥ 18 years old, hospitalized for typical AFI ablation were screened. Typical AFI was diagnosed from the surface 12 lead ECG displaying negative saw-tooth F waves in the inferior leads and positive F waves in lead V1 (14). The following exclusion criteria were applied: inability to communicate with the hypnotherapist such as absence of French language speaking, severe hearing impairment, cognitive impairment, significant psychiatric impairment, or chronic pain interfering with the evaluation of

procedure-related pain. The study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by an ethics committee (Comité de Protection des Personnes 2017-A01267-46). All patients included in this study provided written informed consent the day before the procedure.

Randomization

Patients were randomized 1:1 by computer to receive hypnosis or placebo on top of the classical analgesia protocol. Patients, physicians and nurses were blinded to the intervention. All patients received local anesthesia, and intravenous morphine if required, according to our institutional protocol.

Institutional analgesia protocol

At our institution, 1 gram of intravenous paracetamol is administered prior to the procedure. Local anesthesia was performed by subcutaneous infiltration of 200 mg of lidocaine in the groin. Throughout the procedure, patients were prompted to evaluate their perception of pain using a validated numeric rating scale (NRS), ranging from 0 (“no pain”) to 10 (“worst pain imaginable”) points, at 5 minute intervals by a nurse (15). Patients were automatically given 1 mg of intravenous morphine by the nurse if NRS was ≥ 5 points. Patients could also request additional analgesia in which case further boluses of 1 mg of morphine were given on demand. As analgesia administration was protocol driven, the physician operator was not involved in the decision process. This protocol was developed and validated with the anesthesiology department and represents the standard of care at our institution. Patients were continuously monitored by non-invasive blood pressure monitoring, oxygen saturation and respiratory rate.

Hypnosis group

Hypnosis was administered by experienced practitioners from the French Hypnosis Association. In order to avoid any disruption to the procedure, hypnotherapists conducted the

session by communicating through headphones given to the patient. None of the staff present in the electrophysiology lab were able to hear or be impacted by the hypnosis protocol. Hypnosis began after surgical-site antisepsis and before local anesthesia was administered. The hypnotherapist conducted a traditional Ericksonian session through 3 phases (16, 17). During the first phase, hypnosis induction was carried out using the fixation method: after general relaxation, patients were invited to focus on a red object to distract them from the local environment. Next, the hypnotherapist invited participants to mentally travel to a pleasant location to feel more comfortable. After induction, the anchoring phase started: hypnosis was deepened by repeating statements involving relaxation and by anchoring the resulting state of deep relaxation with repeated key words, leading to a trance-like state. A trance-like state was achieved when the patient was seen to blink more slowly, their eyelids fluttered, muscles were relaxed, and breathing slowed. If this state was not achieved, the hypnotherapist switched to the conversational hypnosis technique, aiming at saturating mind with numerous questions (17–19). The third phase involved waking up, which consisted of a slow return to a non-hypnotic state, actively orchestrated by the hypnotherapist and usually occurring within minutes.

Placebo-controlled group

Patients randomized to the placebo arm were prepared in an identical manner and were also equipped with headphones. Instead of undergoing hypnosis, they received non-hypnotic relaxation suggestions and listened to white noise through headphones (15, 20, 21).

Cavotricuspid AFI ablation procedure

Briefly, the procedure was performed with coronary sinus catheter, halo catheter and an 8-mm non-irrigated tip ablation catheter (Therapy, Abbott, Minneapolis, MN). Cavo-tricuspid isthmus dependency was confirmed by entrainment manoeuvres if applicable. Ablation was carried out at 60 watts, 60 degrees in a continuous lesion set. The endpoint of the procedure

was durable bi-directional block across the ablation line as determined by conventional pacing manoeuvres (22, 23).

Endpoints and Data Collection

The primary end point was the level of pain perception during the procedure as a whole, quantified by patients using a visual analog scale (VAS) score 45 minutes after procedure end (13). The VAS is a 10 centimeters length horizontal line, anchored by 2 verbal descriptors: “no pain” (0 point) and “worst imaginable pain” (10 points), with 1 point every centimeter. Participants were asked to mark a point along the scale that represented a single value of the average pain intensity experienced during the procedure (15). The secondary endpoints were: i) Self-reported pain evaluated every 5 minutes during the procedure with a Numeric rating scale score (NRS) (evolution of pain with time and mean pain reported throughout the procedure); ii) Morphine consumption (in mg) during the procedure; iii) External evaluation of patients’ sedation during the procedure, assessed by the operator evaluating the NRS throughout the procedure; iv) Patient’s anxiety self-assessment during the ablation, evaluated 45 minutes after the procedure by a similar VAS score.

The length of the procedure, radiation duration, dose area product (min and $\text{cGy}\cdot\text{cm}^2$), and procedural complications (severe hypotension, bradycardia, oxygen desaturation, cardiac arrest, pericardial effusion, complete atrioventricular block) were recorded. The length of procedure was considered between surgical-site antisepsis and sheath removal and comprised the duration of hypnosis. Oxygen desaturation was defined as a sustained drop in SpO_2 $<90\%$ for at least 30 seconds (24). Severe hypotension was defined as a drop in systolic blood pressure under 90 mmHg requiring fluid therapy or vasopressor administration. Bradycardia was defined as a heart rate <40 beats per minute.

Medical history and baseline characteristics at inclusion were collected. Baseline anxiety was assessed the day before the ablation using a VAS score and the validated APAIS

score (17). Left ventricular ejection fraction was assessed by transthoracic echocardiography performed in the month prior to ablation. Coronary artery disease was defined by any documented coronary stenosis > 70% in at least one of the three main coronary arteries, with or without a history of myocardial infarction and/or revascularization. Cardiovascular medications such as beta-blocker, amiodarone, calcium inhibitor, anticoagulant or anti-platelet therapy were collected. Anticoagulation was managed according to international Guidelines (25). A 12-lead ECG, hemoglobin (g/dL), serum creatinine ($\mu\text{mol/L}$), and N-terminal pro B-type Natriuretic Peptide (ng/L) were all taken the day before ablation.

Statistical Analysis

The trial was designed to investigate the potential superiority of hypnosis compared to placebo to reduce pain self-assessed by VAS score during AFI ablation. We calculated that 48 patients per group would be sufficient to demonstrate a difference of 2 ± 3 points in VAS score with a power of 0.8 and an alpha level of 0.05 (26). Taking into account a 20% of refusal or inability to participate, 58 patients per group were required which represented a total of 116 patients. Continuous variables were expressed as mean and standard deviation or median and interquartile range if non parametric. Categorical variables were presented as numbers and percentages. Comparisons between groups were performed using Student t-tests or Mann-Whitney U tests for continuous variables as appropriate, and Chi² test for categorical variables. For comparing subtypes of hypnosis techniques (Ericksonian and Conversational) and placebo, the ANOVA with Tamhane correction test was used. Analyses were performed using SPSS 22 (SPSS, Inc., Chicago, IL, USA) and SAS 9.3 (SAS Institute, Inc., Cary, NC, USA) statistical software.

RESULTS

Screening and Eligibility

From October 2017 to September 2019, all consecutive patients with typical AFl were screened for eligibility. Among the 124 patients with typical AFl, 8 (6.5%) patients were not included because of foreign language speaking only (n=2), deaf (n=1), cognitive impairment (n=1), and 4 patients declined study enrollment (n=4).

Baseline Characteristics of Patients

Among the 116 patients included in the study, 3 (2.6%) were excluded, due to withdrawal of study consent before the ablation in 1 patient and conversion to atrial fibrillation in 2 patients requiring a change in therapeutic approach.

Among the 113 patients analyzed, mean age was 69.6 ± 11.9 years, 24 (21%) were females and 28 (25%) had coronary artery disease. Patients were randomized to the Hypnosis group (n=56) or the Placebo group (n=57) (Figure 1). Table 1 illustrates the baseline characteristics of the patients, according to their allocated treatment group. None of the patients underwent a prior electrophysiology procedure. No significant differences were found between the 2 groups in terms of age, gender, NYHA functional class, presence of coronary artery disease, left ventricular ejection fraction, or medications. Anxiety assessment the day before the ablation was 10.8 ± 5.0 vs 10.4 ± 5.6 points (P=0.51) using the APAIS score; and 3.8 ± 3.2 vs 4.8 ± 2.5 points; (P=0.07) using the VAS, in the Hypnosis and Placebo group respectively.

Hypnosis Versus Placebo: Pain and Anxiety Evaluation

There was no significant difference regarding VAS score for anxiety evaluation during the whole procedure between groups (1.5 ± 2.2 vs 2.5 ± 3.2 points; P=0.16 for Hypnosis and Placebo group respectively).

Pain perception was consistently lower in the Hypnosis group as compared with the Placebo group, throughout the procedure by both methods of evaluation (Table 2). At 45 minutes after the end of AFl ablation, the VAS score summarizing the overall pain felt during

the procedure was significantly lower in the Hypnosis group compared to the Placebo group (4.0 ± 2.2 vs 5.5 ± 1.8 points; $P < 0.001$) (Figure 2). Prospective pain rating using the NRS at 5 minute intervals during the procedure, was also significantly lower in the Hypnosis group as compared with Placebo group: 1.7 ± 1.4 vs 3.6 ± 1.8 points respectively; $P < 0.001$. Moreover, pain was consistently lower at every time point during the procedure in the Hypnosis group, as illustrated in Figure 3. Patients' external evaluation of sedation during the procedure was significantly better in the Hypnosis group compared to Placebo group (8.3 ± 2.2 vs 5.4 ± 2.5 points; $P < 0.001$), in line with patient's self-assessment.

Finally, 34 (61%) patients required morphine injection in the Hypnosis group versus 53 (93%) in the Placebo group; $P < 0.001$. Further, the dose of morphine was significantly lower in the Hypnosis group as compared to the Placebo group (1.3 ± 1.3 mg vs 3.6 ± 1.8 mg respectively; $P < 0.001$).

Hypnosis Versus Placebo: Procedural Success and Complications

There was no difference in procedure duration between groups (35.5 ± 10.3 min in the Hypnosis group and 36.6 ± 12.1 min in the Placebo group; $P = 0.82$). There was a trend to radiofrequency application duration decrease in the Hypnosis group: 522 ± 330 vs 586 ± 291 sec in the Placebo groups ($P = 0.06$). Total fluoroscopy duration and dose area product were not significantly different between groups: 9.5 ± 5.9 vs 9.7 ± 5.2 min ($P = 0.91$) and 702 ± 784 vs 619 ± 632 cGy*cm² ($P = 0.50$) in the Hypnosis and Placebo groups respectively.

Procedural success, defined as bi-directional block across the cavo-tricuspid isthmus, was achieved in 55 (96.4%) patients of the Hypnosis group and 52 (91.2%) patients of the Placebo group ($P = 0.44$). Finally, no complication occurred in the Hypnosis group versus 6 (11%) in the Placebo group ($P = 0.03$). These were pericardial effusion (n=1), oxygen desaturation (n=1) and severe hypotension related to morphine administration (n=4).

Response to type of hypnosis

Among the 56 patients assigned to the Hypnosis group, 36 (64%) responded to traditional Ericksonian hypnosis, while 20 (36%) were shifted to Conversational hypnosis because of their lack of receptiveness to traditional hypnosis. Median age and gender were not different between those two subgroups (71 [IQR 63; 75] years and 72 [IQR 62; 76] years ; P=0.69 and 83.3% males vs. 65% males ; P=0.17 in the Ericksonian and Conversational subgroups respectively).

Regarding pain evaluation and morphine consumption, the Ericksonian group was significantly better than placebo on all parameters. Comparisons between Eriksonian, Conversational and placebo groups are shown in Table 3. The overall VAS score for pain during the whole procedure was 6 [IQR 4; 7] in the placebo group, 4 [IQR 2; 5] in the Ericksonian group and 4.5 [IQR 2; 6] in the Conversational group (P=0.002). Both hypnosis methods resulted in lower NRS score, better sedation and lower morphine requirements than placebo. However, procedure duration in the Conversational group was higher, although this did not reach statistical significance (35 [IQR 26; 42] min in the Placebo group, 34 [IQR 25.5; 39.75] min in the Ericksonian group and 42.5 [IQR 30.3;50] min in the Conversational group; P=0.09. Further, radiofrequency duration was significantly lower in the Ericksonian group compared to placebo (P<0.01).

DISCUSSION

This is the first randomized study assessing the efficacy of hypnosis on pain perception during ablation of typical AFl. Compared to controls, patients randomized to the Hypnosis group had significantly reduced pain, lower morphine requirements, and fewer complications.

Hypnosis Benefits

The first randomized study assessing the positive effects of hypnosis regarding pain reduction was published in 2000 in patients undergoing percutaneous vascular and renal procedures

(27). However, its use in clinical practice is not widespread and opioid analgesia remains the standard of care in these patients, who often require substantial doses for effective pain relief.

Our study demonstrates the superiority of hypnosis compared to placebo in reducing the perception of pain, and lower morphine requirements. Several methods for pain assessments were used to ensure the consistency and reproducibility of the results. The prospective evaluation of pain every 5 minutes throughout the procedure showed that hypnosis was effective from the onset of the procedure and persisted throughout. Indeed, NRS scores were significantly lower in the Hypnosis group from the beginning to 35 minutes (mean duration of the AFI procedure). The absence of statistical difference from 35 min onwards may be due to a lack of power given that procedures being concluded earlier, reduced the sample size. Moreover, our results are consistent with previously published data on the use of hypnosis during atrial fibrillation ablation using a NRS score: mean score of 1.7 ± 1.4 points in our study and 1.3 ± 1.6 points in the literature (12). Finally, we showed a significant reduction in morphine consumption in the Hypnosis group, which supports that hypnosis may also alleviate pain in itself. Consistent with this, two studies showed that hypnosis could reduce morphine requirements by 2.5-fold after coronary artery bypass grafting and prostate brachytherapy (28, 29).

One may postulate that the analgesic effect of hypnosis may be partly due to anxiety reduction, as previously reported (30). However, we found no significant difference in the level of reported anxiety between groups, neither in the preoperative assessment nor during the procedure. However, white noise and non-hypnotic suggestions experienced by controls may, in themselves, decrease anxiety during the procedure. The very low levels of self-reported anxiety in both groups are in line with this hypothesis.

Hypnosis May Limit Morphine-Related Complications

Opioids are frequently used either solely or in combination with benzodiazepines for sedation in electrophysiology procedures (6). They may cause frequent and sometimes serious complications, including cardiac arrest related to respiratory depression (9). In this study, hypnosis significantly decreased morphine consumption and therefore the risk of opioid-related complications. It has been shown that the risk of adverse events is associated with the dose of opioids received by the patients (31). In our study, 93% of patients in the Placebo group required morphine versus 61% in the Hypnosis group, this result being more evident in the patients who responded well to initial attempts at hypnosis (Ericksonian hypnosis), in which only 47% of patients needed morphine ($P < 0.001$). This highlights the outcome differences between the Ericksonian and the Conversational groups which may be due to several reasons. Conversational hypnosis can be considered a “second chance” after the Ericksonian technique failed. Furthermore, there is no reliable manner to objectively assess failures with Conversational hypnosis, as it does not induce trance-like state per se. Therefore, the Conversational hypnosis group comprised more patients refractory to hypnosis. Patients in the Placebo group received three times the dose of morphine than patients in the Hypnosis group, and as a consequence, had a higher rate of opioid related complications (respiratory depression and symptomatic hypotension). This is of particular importance for elderly patients with major comorbidities undergoing ablation, who are at increased risk of complications from opioids. Nevertheless, this difference in opioid-related adverse events should be confirmed in larger studies.

Hypnosis Implementation in The Standard of Care

Availability of general anesthesia is becoming increasingly difficult in many electrophysiology units. General anaesthesia is time consuming, associated with added risk and has a longer recovery period. Therefore, alternative solutions may be advantageous in this setting. In this study, hypnosis negated the need for morphine administration in more than

half of the good-respondents, and even when required the dose was significantly lower. Moreover, the total procedure duration was not lengthened in the hypnosis group; on the contrary, radiofrequency ablation duration was shorter in the Ericksonian group than in the control group. This may be related to a better analgesia with hypnosis, leading to more comfort for the patient and in turn, better catheter stability during ablation. As detailed in Table 3, not all patients responded well to the Ericksonian technique, and a third of patients needed to switch to Conversational hypnosis. In this subgroup, the analgesic effect of hypnosis was reduced, but patients still reported better pain control than in the placebo arm. Therefore, there may be a role for screening of patients prior to the procedure based on their responsiveness to the type of hypnosis. This was not implemented in this study, in order to investigate the results in a real-world unselected population. However, this can be easily incorporated into pre-existing protocols in future which may further reduce the procedure time. Finally, hypnosis can be easily implemented in the electrophysiology laboratory. In our electrophysiology department, 2 nurses have undertaken a seven-day training course delivered by the French Society of Hypnosis and were able to deliver this alternative technique in AFI ablation and we have expanded this to other procedures.

Limitations

The single-centre design of the study may be a limitation. However, it ensures homogeneity in the care of patients, in particular all the procedures have been performed by the same interventional team under the same conditions. Although the placebo intervention was carefully designed by the hypnotherapist to minimize the chance that participants would know which arm they were assigned to. It may have still been possible for patients in the placebo group to suspect that white noise and suggestions were not hypnotic in nature. The protocol was strictly adhered to and at no point during the study were patients informed which arm they were assigned to. Given the very low anxiety levels reported during the procedure, we

are confident that the blinding process and choice of placebo were effective. However, we did not ascertain in which group the patients thought they were allocated to, after the procedure. Finally, pain assessment is subjective by nature, and no evaluation technique can completely eliminate this bias. However, the multi modal assessment of pain and sedation allowed for a more reproducible analysis of the impact of hypnosis.

CONCLUSION

In this first randomized trial of unselected patients undergoing ablation of typical AFI, hypnosis significantly reduced perceived pain and morphine consumption when compared to controls receiving non-hypnotic suggestions and white noise. Complications related to opioid use were significantly lower in patients receiving hypnosis. Hypnosis is an effective adjunct to analgesia in reducing pain perception and may eliminate the need for intravenous opioids and their associated risks.

PERSPECTIVES

Patient Care and Procedural Skills

Hypnosis is effective for management of pain during atrial flutter ablation and is associated with reduced pain and morphine requirements compared to placebo.

Translational Outlook

Additional randomized trials are needed to

1. Determine whether pre-selection of patients receptive to hypnosis prior to ablation is a relevant strategy in the setting of standard of care implementation.
2. Determine whether hypnosis is effective for other ablation procedures such as atrial fibrillation ablation

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FIGURE LEGENDS

Figure 1: Flow-Chart.

Patients were randomly assigned to either a hypnosis or placebo in a 1:1 ratio. Only 3 randomized patients were not analyzed (2 from the Hypnosis group and 1 from the Placebo group).

Figure 2: Visual Analog Scale Score for Global Pain and Morphine Requirements During Procedure.

A. Compared to the Placebo group, patients from the Hypnosis group presented significantly lower VAS score assessing global pain. B. Morphine requirements were significantly lower in the Hypnosis group compared to the Placebo group.

Figure 3: Numeric Rating Scale Assessing Pain During Atrial Flutter Ablation in the Hypnosis and Placebo Group.

Median and interquartile range are expressed. Star indicates a P value <0.05. Median numeric rating scale was lower in the Hypnosis group compared to the Placebo group from the start of the procedure up till 35 minutes. Then, there was no significant difference between groups.

Figure 4: Central illustration

The PAINLESS study assessed the superiority of Hypnosis versus Placebo regarding pain perception and opioid consumption during atrial flutter ablation. Pain self-assessment using a validated visual analog scale was significantly lower in the Hypnosis group (4.0 ± 2.2 points vs 5.5 ± 1.8 4; $P < 0.001$). Morphine consumption was significantly lower in the Hypnosis group compared to the Placebo group (1.3 ± 1.3 mg vs 3.6 ± 1.8 mg respectively, $P < 0,001$).

TABLES

Table 1: Baseline Patients Characteristics

| | Hypnosis group n=56 | Placebo group n=57 | P-value |
|--|------------------------|-----------------------|---------|
| Age, years | 69.6 ±11.7 | 69.4 ±12.2 | 0.96 |
| Male | 43 (77) | 46 (81) | 0.61 |
| Height, cm | 171 ±10 | 172 ±9 | 0.71 |
| Weight, kg | 86.7 ±19.0 | 84.0 ±19.9 | 0.30 |
| NYHA fonctionnal class | | | |
| Class I-II | 39 (70) | 45 (79) | 0.56 |
| Class III-IV | 17 (30) | 12 (21) | |
| Hypertension | 38 (68) | 32 (56) | 0.20 |
| Diabetes | 13 (23) | 11 (19) | 0.61 |
| Smoking | 17 (30) | 14 (25) | 0.49 |
| Hypercholesterolemia | 24 (43) | 24 (42) | 0.94 |
| Atrial fibrillation | 18 (32) | 16 (28) | 0.64 |
| CHA ₂ DS ₂ -VASc score | 2.5 ±1.3 | 2.4 ±1.7 | 0.52 |
| Coronary artery disease | 16 (29) | 12 (21) | 0.36 |
| Systolic blood pressure, mmHg | 133 ±23 | 138±24 | 0.37 |
| Heart rate, bpm | 85 ±26 | 81 ±23 | 0.46 |
| Stroke | 6 (11) | 2 (4) | 0.16 |
| LVEF, % | 55 ±13 | 56 ±10 | 0.81 |
| ECG rhythm | | | |

| | | | |
|-------------------------------|-----------|------------|------|
| sinus rhythm | 17 (30) | 16 (28) | 0.79 |
| typical flutter | 39 (70) | 41 (72) | |
| Hemoglobin, g/dL | 13.4 ±2.0 | 13.9 ±1.7 | 0.08 |
| Creatinin, µmol/L | 102 ±38 | 96 ±26 | 0.49 |
| NT-proBNP, ng/l | 976 ±997 | 1001 ±1540 | 0.25 |
| Medication | | | |
| anticoagulant | 51 (91) | 54 (94) | 0.49 |
| beta-blockers | 39 (70) | 41 (72) | 0.79 |
| diuretics | 21 (38) | 19 (33) | 0.64 |
| ACEi | 32 (57) | 31 (54) | 0.77 |
| antiplatelet agents | 16 (29) | 14 (25) | 0.71 |
| amiodarone | 12 (21) | 10 (18) | 0.60 |
| Pre-operative APAIS score | 10.8 ±5.0 | 10.4 ±5.6 | 0.51 |
| VAS for pre-operative anxiety | 3.8 ±3.2 | 4.8 ±2.5 | 0.07 |

Results are expressed as mean and standard deviation or number (%).

Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; ECG: electrocardiogram; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro B-type Natriuretic Peptide NYHA: New-York Heart Association

TABLE 2: Pain, Anxiety and Morphine Requirements Comparison in Hypnosis and Placebo Groups.

| | Hypnosis group n=56 | Placebo group n=57 | P value |
|-------------------------------------|------------------------|-----------------------|---------|
| VAS for pain during whole procedure | 4.0 ±2.2 | 5.5 ±1.8 | <0.001 |
| NRS prospective pain rating | 1.7 ±1.4 | 3.6 ±1.8 | <0.001 |
| VAS for worst pain | 6.3 ±2.7 | 7.6 ±1.9 | 0.01 |
| VAS for perprocedural anxiety | 1.5 ±2.2 | 2.5 ±3.2 | 0.16 |
| External evaluation of sedation | 8.3 ±2.2 | 5.4 ±2.5 | <0.001 |
| Patients requiring morphine | 34 (61) | 53 (93) | <0.001 |
| Morphine dose, <i>mg</i> | 1.3 ±1.3 | 3.6 ±1.8 | <0.001 |
| Procedure duration, <i>min</i> | 35.5 ±10.3 | 36.6 ±12.1 | 0.82 |
| Radioscopy duration, <i>min</i> | 9.5 ±5.9 | 9.7 ±5.2 | 0.91 |
| Dose area product, <i>cGy*cm2</i> | 702 ±784 | 619 ±632 | 0.50 |
| Radiofrequency duration, <i>sec</i> | 522 ±330 | 586 ±291 | 0.06 |

Results are expressed as mean and standard deviation or number (%). Abbreviations: NRS numeric rate scale; VAS visual analog scale

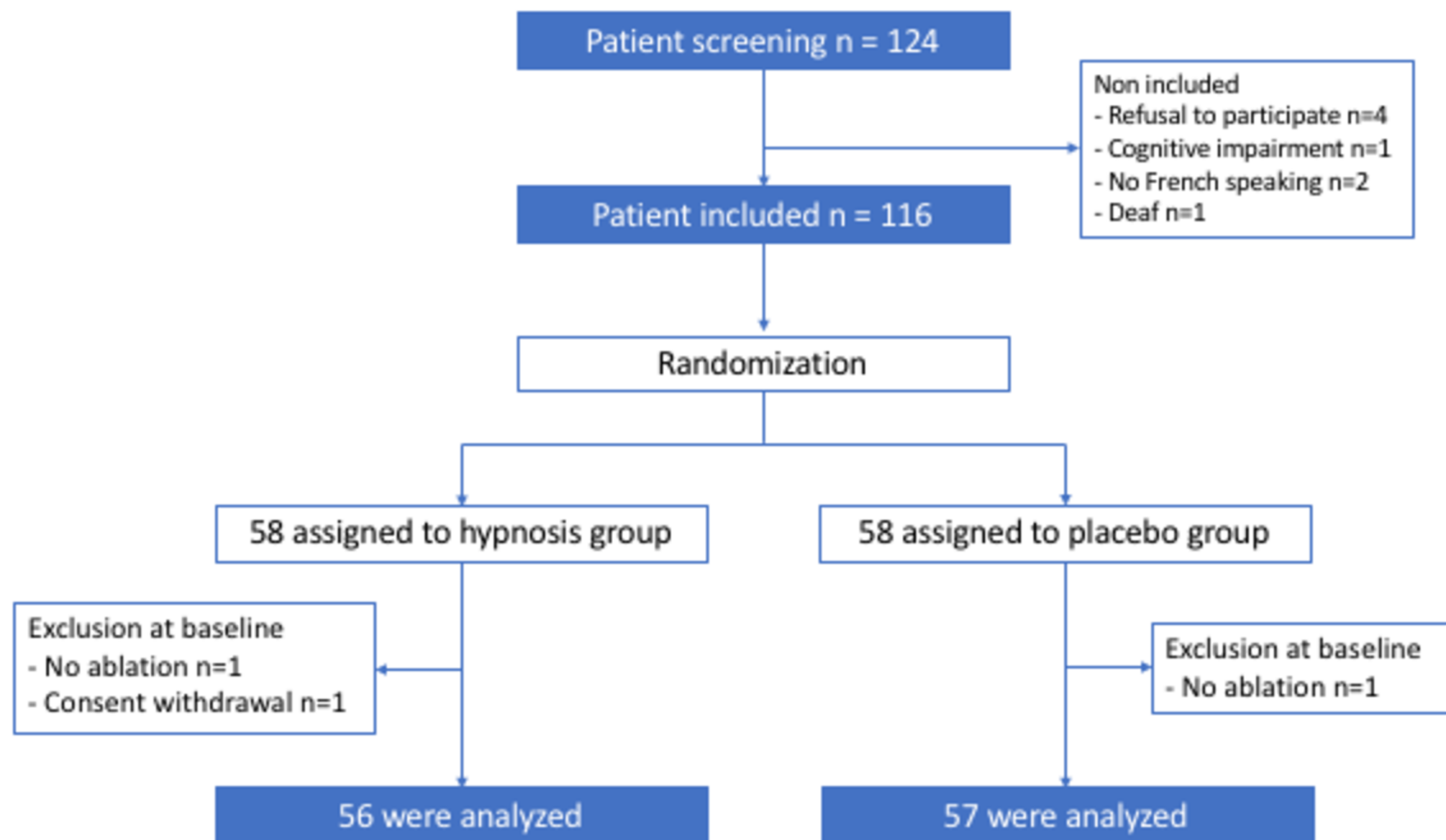
TABLE 3: Comparison According to the Different Types of Hypnosis

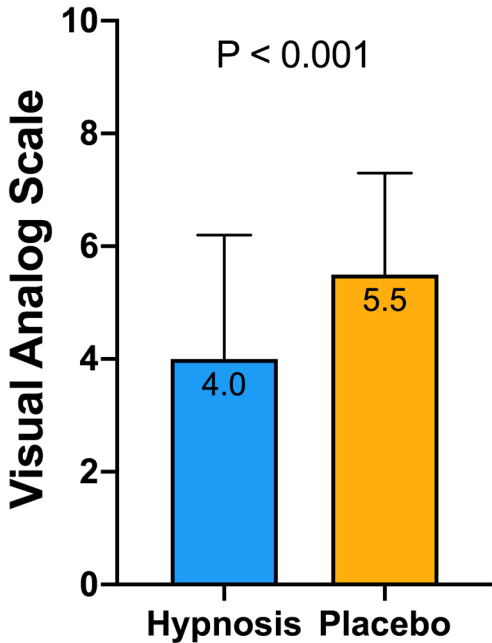
| | Placebo | Ericksonian hypnosis n=57 n=36 | Conversational hypnosis n=20 | Global P Value | Tahmane P value Ericksonian hypnosis vs Placebo | Tamhane P value Conversational hypnosis vs Placebo |
|-------------------------------------|----------------|---|------------------------------------|-------------------|---|--|
| VAS for pain during whole procedure | 6 [4; 7] | 4 [2; 5] | 4.5 [2; 6] | 0.002 | <0.001 | 0.11 |
| NRS prospective pain rating | 5.3 [3.6; 6.3] | 1.3 [0.1; 2.3] | 3.6 [2.5; 4.0] | <0.001 | <0.001 | <0.01 |
| VAS for worst pain | 8 [6.5; 9] | 6.5[4.25; 8] | 8 [5.25; 9] | 0.01 | 0.01 | 0.69 |
| External evaluation of sedation | 6 [3; 8] | 10 [8; 10] | 6.5 [5; 9] | <0.001 | <0.001 | 0.14 |
| Patients requiring morphine | 53 (93) | 17 (47) | 17 (85) | <0.001 | <0.001 | 0.29 |
| Morphine dose, <i>mg</i> | 4 [2; 4] | 0 [0; 2] | 2 [1; 2.75] | <0.001 | <0.001 | <0.001 |
| Procedure duration, <i>min</i> | 35 [26; 42] | 34 [25.5; 39.75] | 42.5 [30.3;50] | 0.09 | 0.17 | 0.73 |

| | | | | | | |
|-------------------------------------|----------------|----------------|-----------------|------|-------|------|
| Fluoroscopy duration, <i>min</i> | 8 [5.7; 14] | 8 [5; 8.8] | 11 [7.06; 13] | 0.05 | 0.18 | 0.38 |
| Dose area product, <i>cGy*cm2</i> | 446 [206; 727] | 439 [289; 698] | 588 [234; 1077] | 0.68 | 0.98 | 0.87 |
| Radiofrequency duration, <i>sec</i> | 501 [389; 759] | 387 [295; 480] | 567 [320; 975] | 0.01 | <0.01 | 0.66 |

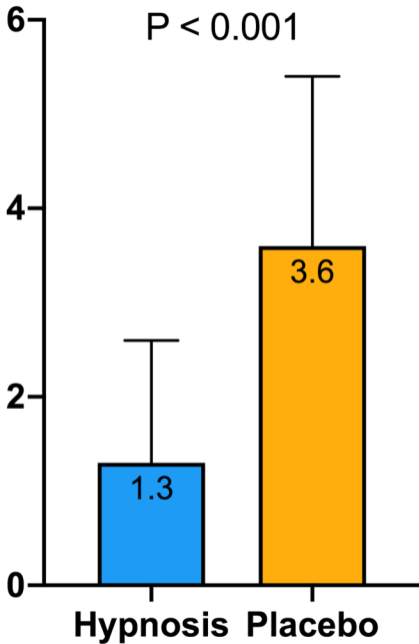
Results are expressed as median and interquartile range or number (%). Abbreviations: NRS numeric rate scale; VAS

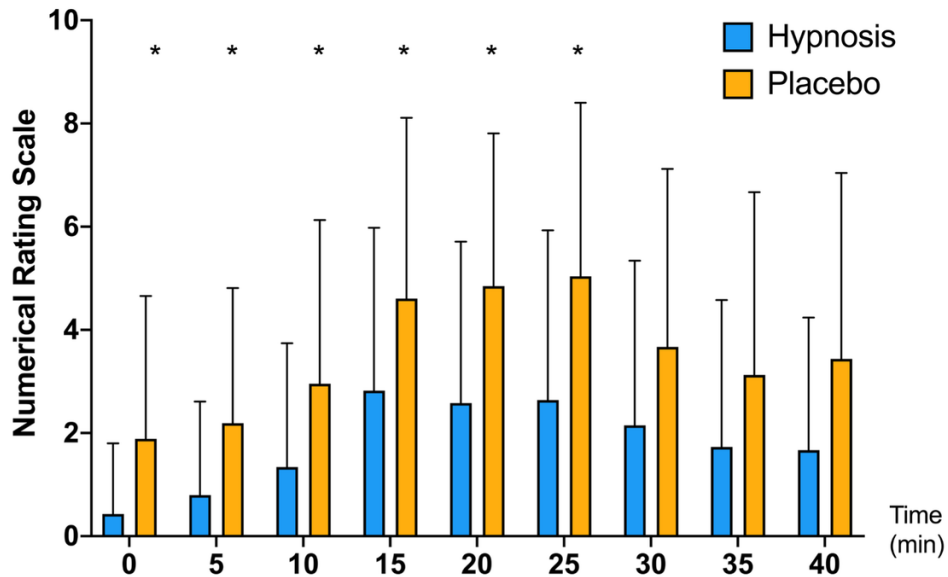
visual analog scale





Morphine (mg)





Nbr subjects

Hypnosis

Placebo

| | | | | | | | | |
|----|----|----|----|----|----|----|----|----|
| 56 | 56 | 56 | 56 | 52 | 45 | 33 | 21 | 11 |
| 57 | 57 | 57 | 57 | 52 | 48 | 41 | 31 | 25 |

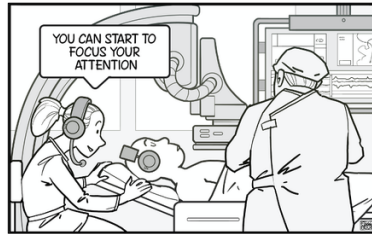
Hypnosis versus Placebo during Atrial Flutter Ablation - The PAINLESS Trial -

RANDOMIZED CONTROLLED TRIAL

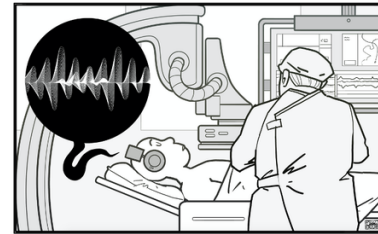
113 patients hospitalized
for Atrial Flutter Ablation



Hypnosis



Placebo



Mean pain score

4.0 ± 2.2

P < 0.001

5.5 ± 1.8

Morphine requirements

1.3 ± 1.3 mg

P < 0.001

3.6 ± 1.8 mg

Hypnosis during Atrial Flutter ablation is superior to placebo for alleviating pain and reducing morphine administration