

Tumescent Technique for Local Anesthesia Improves Safety in Large-Volume Liposuction

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The tumescent technique for local anesthesia improves the safety of large-volume liposuction (≥ 1500 ml of fat) by virtually eliminating surgical blood loss and by completely eliminating the risks of general anesthesia. Results of two prospective studies of large-volume liposuction using the tumescent technique are reported.

In 112 patients, the mean lidocaine dosage was 33.3 mg/kg, the mean volume of aspirated material was 2657 ml, and the mean volume of supranatant fat was 1945 ml. The mean volume of whole blood aspirated by liposuction was 18.5 ml. For each 1000 ml of fat removed, 9.7 ml of whole blood was suctioned. In 31 large-volume liposuction patients treated in 1991, the mean difference between preoperative and 1-week postoperative hematocrits was -1.9 percent. The last 87 patients received no parenteral sedation.

In a second study, a 75-kg woman received 35 mg/kg of lidocaine on two separate occasions, first without liposuction and 25 days later with liposuction; peak plasma lidocaine concentrations occurred at 14 and 11 hours after beginning the infiltration and were 2.37 and 1.86 $\mu\text{g/ml}$, respectively. (*Plast. Reconstr. Surg.* 92: 1085, 1993.)

Among the greatest risks of liposuction surgery are the dangers associated with general anesthesia and excessive bleeding.^{1,2} Utilizing copious volumes of very dilute lidocaine, the tumescent technique for liposuction eliminates or minimizes these risks. It permits liposuction of more than 3000 ml of fat totally by local anesthesia without sedation. The estimated maximum safe lidocaine dosage using the tumescent technique is 35 mg/kg.³

This paper presents data showing that the tumescent technique for large-volume liposuc-

tion not only eliminates the need for general anesthesia, IV sedation, and narcotic analgesics but also virtually eliminates surgical blood loss.

PATIENTS AND METHODS

One-hundred and twelve patients who had liposuction of at least 1500 ml of supranatant fat from February of 1989 through October of 1992 were included in this prospective study. All patients were treated as outpatients in an office-based surgical facility or in a state-licensed multispecialty ambulatory surgicenter. None of the patients was hospitalized.

Patients were prescribed antibiotics, cefadroxil, 500 mg, or doxycycline, 100 mg, taken twice daily for 6 days, beginning the day before surgery. No narcotic analgesics were used in any patient. As a safety precaution, all patients had an IV line for infusion of physiologic saline to maintain vascular access.

Flurazepam, 30 mg, the night before surgery or the morning of surgery, was available to all patients, although only a few took it. In 1991, the routine use of parenteral sedation was discontinued. Because of anxiety, 1 of 40 patients treated in 1991 required IV sedation, receiving a total of two 1-mg doses of IV medazolam. None of the last 87 patients received any IV or IM sedation.

Anesthesia was achieved by direct infiltration into subcutaneous fat of a solution of lidocaine, 400 to 1000 mg, epinephrine, 0.5 to 1.0 mg, and sodium bicarbonate, 10 mEq in 1 liter of phys-

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iologic saline. Beginning in late 1991, triamcinolone, 10 mg/liter, was added to the anesthetic solution (Table I). A motor-driven peristaltic pump (Wells-Johnson Company, Tucson, Ariz.) permitted efficient infiltration into subcutaneous fat at rates of 50 to 200 ml/min depending on the patient's tolerance and the area of infiltration. Infiltration was accomplished with a 20-gauge spinal needle, an 18-gauge intradiscal needle, and a blunt-tipped two-hole 14-gauge infiltrating cannula. The entire infiltration process was completed before starting liposuction.

The liposuction cannulas were made from fully hard-tempered stainless steel hypodermic needle stock in 12 gauge = 2.47 mm inside diameter (ID) and 10 gauge = 3.10 mm ID. Small cannulas permit efficient liposuction both deeply and superficially and, together with the tumescent technique, minimize the risk of surgically induced irregularities of the skin. Details of the operative technique have been described.⁴ Liposuction was accomplished with the assistance of a Wells-Johnson Aspirator II medical-grade vacuum pump.

The volume of whole blood aspirated by liposuction, $Vol_{ASPIRATED\ WHOLE\ BLOOD}$, was calculated with the following equation:

$$Vol_{ASPIRATED\ WHOLE\ BLOOD} = \frac{[(Vol_{INFRA}) + (0.16)(Vol_{SUPRA})] \times Hct_{INFRA}}{Hct_{VENOUS\ BLOOD}}$$

where

- $Hct_{VENOUS\ BLOOD}$ = Preoperative hematocrit of venous whole blood
- Hct_{INFRA} = Hematocrit of the infranatant blood-tinged anesthetic solution removed by liposuction
- Vol_{INFRA} = Volume of the infranatant blood-tinged anesthetic solution removed by liposuction measured after separation by gravity for at least 30 minutes
- Vol_{SUPRA} = Volume of the supranatant fat, defined as the volume of fat that is measured after separation by gravity for at least 30 minutes

TABLE I

Recipe for the Tumescent Technique Anesthetic Solution for Liposuction

Lidocaine	Epinephrine
500 mg (0.05%) with	0.5 mg (1:2 million) <i>or</i>
750 mg (0.75%) with	0.75 mg (1:1.5 million) <i>or</i>
1000 mg (0.1%) with	0.75 mg (1:1.5 million)
Sodium bicarbonate	10 mEq (10 ml of 8.4% NaHCO ₃)
Triamcinolone	10 mg (an optional ingredient)
Physiologic saline	1000 ml of 0.9% NaCl

When 10-ml samples of gravity-separated supranatant fat are centrifuged for 5 minutes, the average separation yields 8.4 ml of pure yellow fat essentially devoid of residual red blood cells and an additional 1.6 ml of blood-tinged anesthetic solution.

All samples of blood were obtained from peripheral veins. Plasma lidocaine levels were measured by high-pressure gas chromatography.⁵ Hematocrit was measured by an automated technique (Sesmex NE 8000 TOA). The expected hematocrit after a 40:1 dilution of venous blood matched the measured hematocrit quite closely, confirming the accuracy of the automated measurement of the hematocrit of the very dilute infranatant fluid.

The following data were recorded: total doses of lidocaine and epinephrine, total volume of IV fluids, preoperative and 1-week postoperative hematocrit, preoperative and immediately postoperative urine specific gravity, intraoperative urine output, and postoperative orthostatic blood pressure and heart rate. The pulse rate and cardiac rhythm were monitored continuously, and electrocardiogram tracings and blood pressure were automatically recorded periodically.

In 31 of the 40 patients treated in 1991, hematocrits were obtained 1 week postoperatively and compared with preoperative values. Of the remaining 9 patients, postoperative hematocrits were not obtained in 5 patients because they declined to participate in the study, in 2 patients because the staff neglected to ask the patients to participate, and in 2 patients because they returned home to a foreign country within 7 days of the surgery.

In the second part of this study, a 75-kg woman received 2625 mg (35 mg/kg) of lidocaine in 5.25 liters of physiologic saline (lidocaine 0.05%, epinephrine 1:2 million, NaHCO₃ 10 mEq/liter) infiltrated subcutaneously, first without liposuction, and then 25 days later, after an identical infiltration, with liposuction. After each infiltra-

TABLE II
Summary of Results for 112 Large-Volume Liposuction Patients

	Mean	Minimum	Maximum
Weight, females	68.6 kg	55.6 kg	100.9 kg
Weight, males	93.1 kg	87.7 kg	98.6 kg
Total lidocaine dosage	33.3 mg/kg	11.0 mg/kg	52.1 mg/kg
Local anesthetic solution	4608.9 ml	2050 ml	7275 ml
IV physiologic saline	429.7 ml	200 ml	1000 ml
Aspirated fat and anesthetic	2657 ml	1840 ml	4575 ml
Aspirated supranatant fat	1945 ml	1500 ml	3400 ml
Aspirated whole blood	18.5 ml	4.0 ml	37.3 ml
Hct change (postop-preop)	-1.9%	-5.2%	+1.3%
Whole blood per liter of supranatant fat	9.5 ml/liter		
Whole blood per liter of aspirate	7.0 ml/liter		

tion, sequential changes in plasma lidocaine concentrations, hematocrit, weight, cumulative urine volumes, and urine specific gravity were measured.

After liposuction of the body using the tumescent technique, patients wear two postoperative unisex elastic support garments until the drainage has ceased, usually in 2 to 5 days.

RESULTS

The 112 patients in the present study, 108 of whom were females, had liposuction of between 1500 and 3400 ml of supranatant fat (Table II). The mean weight for females was 68.6 kg (range 55.6 to 100.9 kg), and for males, 93.1 kg (range 87.7 to 98.6 kg). The mean total lidocaine dosage was 33.3 mg/kg (range 11.0 to 52.1 mg/kg) (Fig. 1).

The mean volume of local anesthetic solution was 4608.9 ml (range 2050 to 7275 ml). The mean volume of intravenous infusion of physio-

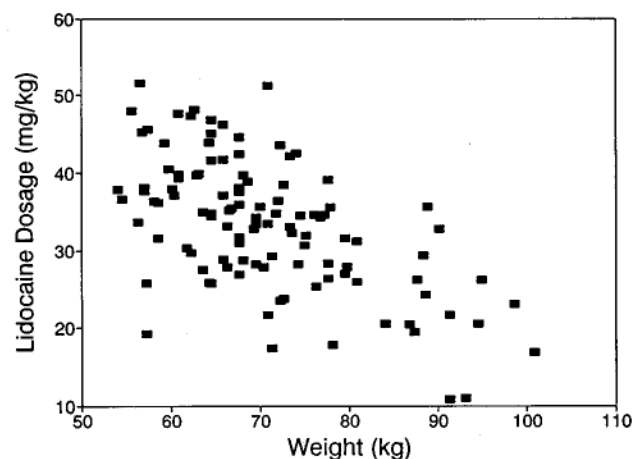


FIG. 1. The distributions of lidocaine dosage (mg/kg) and preoperative weight (kg) in the 90 patients who had large-volume liposuction using the tumescent technique. There was no clinical evidence of lidocaine toxicity in any of these patients. Patients who weighed the least tended to receive higher dosages of lidocaine.

logic saline given during the surgery was 429.7 ml (range 200 to 1000 ml).

The mean volume of aspirate (supranatant fat plus infranatant blood-tinged anesthetic solution) was 2657 ml (range 1840 to 4575 ml), of which the mean volume of supranatant fat was 1945.1 ml (range 1500 to 3400 ml) (Fig. 2).

The mean preoperative hematocrit was 40.8 percent, and the mean postoperative hematocrit was 38.9 percent, with the mean change being -1.9 percent (range -5.2 to +1.3 percent). For each liter of supranatant fat removed by liposuction, there was only a 1 percent change in hematocrit. The calculated mean volume of aspirated whole blood was 18.5 ml (range 4.0 to 37.3 ml). The mean volume of whole blood removed by liposuction was 9.5 ml per liter of supranatant fat. The mean volume of whole blood was 7.0 ml per liter of aspirated material (Fig. 2).

No patient received a blood transfusion or intravascular fluid expanders. There were no serious complications. There were no infections, no episodes of clinical hypovolemia, no adverse drug reactions, no seromas, and no hematomas. Aesthetic results were good and within the patients' range of expectations.

Postoperatively, the mean supine and standing systolic blood pressures were 119 and 121 mmHg, respectively; the mean supine and standing diastolic blood pressures were 71 and 72 mmHg, respectively; the mean supine and standing pulse rates were 88 and 96 beats per minute, respectively. Preoperative and postoperative urine specific gravities were 1.020 and 1.016, respectively. The mean cumulative intraoperative urine volume was 575 ml.

The mean preoperative pulse rate was 72.6 beats per minute, and the mean immediately postoperative pulse rate was 85.1 beats per minute. The range of the difference between

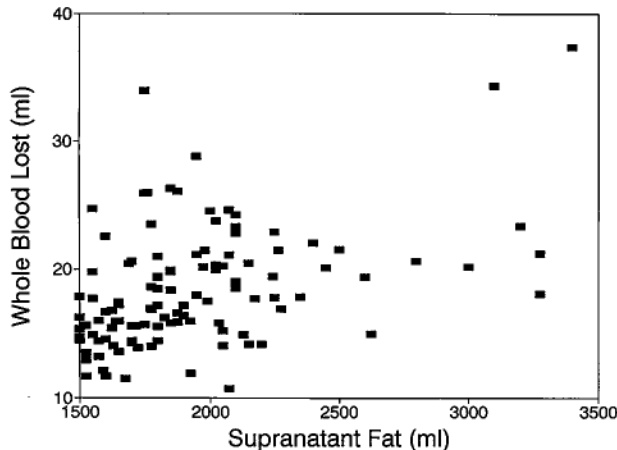


FIG. 2. The distributions of the volume of whole blood and the volume of supranatant fat removed during large-volume liposuction using the tumescent technique.

preoperative and postoperative pulse rates was -14 and 33 beats per minute.

In the second part of this study, a peak lidocaine plasma concentration of $2.37 \mu\text{g}/\text{ml}$ was achieved 14 hours after the infiltration was begun in a 75-kg woman who was given 2625 mg ($35.0 \text{ mg}/\text{kg}$) of lidocaine in 5.25 liters of physiologic saline infiltrated subcutaneously without liposuction.

Twenty-five days later, after an identical infiltration, the patient had liposuction of 1550 ml of supranatant fat. In this instance, the peak lidocaine plasma level of $1.86 \mu\text{g}/\text{ml}$ was attained 11 hours after initiating the infiltration. The peak lidocaine level following liposuction was 78.5 percent of the peak attained without liposuction.

After each infiltration there was a significant sequential change in hematocrit, with the hemodilution caused by the large volume of anesthetic solution infiltrated subcutaneously. Liposuction had little effect on the hematocrit during and after surgery. Adequate intraoperative urine volume, low urine specific gravity, and minimal postoperative differences between supine and standing pulse rates suggest that liposuction using the tumescent technique caused no deficit of intravascular fluid volume (Fig. 3).

DISCUSSION

The tumescent technique for liposuction totally by local anesthesia without sedation was developed by surgeons who traditionally do not use general anesthesia. The description of the tumescent technique has appeared almost exclusively in the literature of dermatology.⁶⁻¹⁰

Large-volume liposuction totally by local anesthesia has not been described in the literature of other specialties.¹⁹⁻²³ The chapter on suction lipectomy in a recent textbook of plastic surgery devoted only one sentence to anesthesia: "Use general anesthesia if: suctioning multiple areas, removing more than 1500 cc of fat, or anticipating autologous blood transfusion (for this an overnight admission is advisable)."²⁴ The tumescent technique used concomitantly with general anesthesia has been described.²⁵⁻²⁷

Advantages of the technique include (1) profound local anesthesia, (2) reduced surgical blood loss, (3) the reduction of IV fluid requirements, and (4) enhanced aesthetic results (Figs. 4 through 6). "Expansion of the fat compartment increases the margin of safety and reduces the likelihood of creating surface irregularities."²⁸

Because there is an increased risk of excessive blood loss when more than 1500 ml is aspirated, autologous blood transfusions have been recommended for liposuction of more than 1500 ml.^{1,29,30} It is this 1500-ml threshold volume that motivates the definition of *large-volume* liposuction. The tumescent technique permits liposuction of more than 3000 ml of supranatant fat without transfusion.

Improved Hemostasis

The degree to which infiltration with vasoconstrictive local anesthetic solutions is used in liposuction to maximize hemostasis varies among different techniques. At one end of the spectrum is the *dry technique*, which uses general anesthesia without infiltration of any vasoconstrictive solution. The official guidelines of the American Academy of Dermatology state that "because of the availability of safer methods, the dry technique is now rarely indicated."³¹ The dry technique is the liposuction technique that causes the greatest degree of blood loss, with between 20 and 45 percent of the aspirate consisting of blood.^{1,2,30-33} In a recent study of 108 patients who had large-volume liposuction (≥ 1500 ml of aspirated fat and blood) by the dry technique, on average, a third of everything that was removed was blood, and every patient was given a blood transfusion.²

The *wet technique*, intermediate with respect to the degree of hemostasis that can be obtained in liposuction, relies on general anesthesia and the use of relatively small volumes of dilute epinephrine infiltrated subcutaneously. With the wet technique, between 15 and 30 percent of the

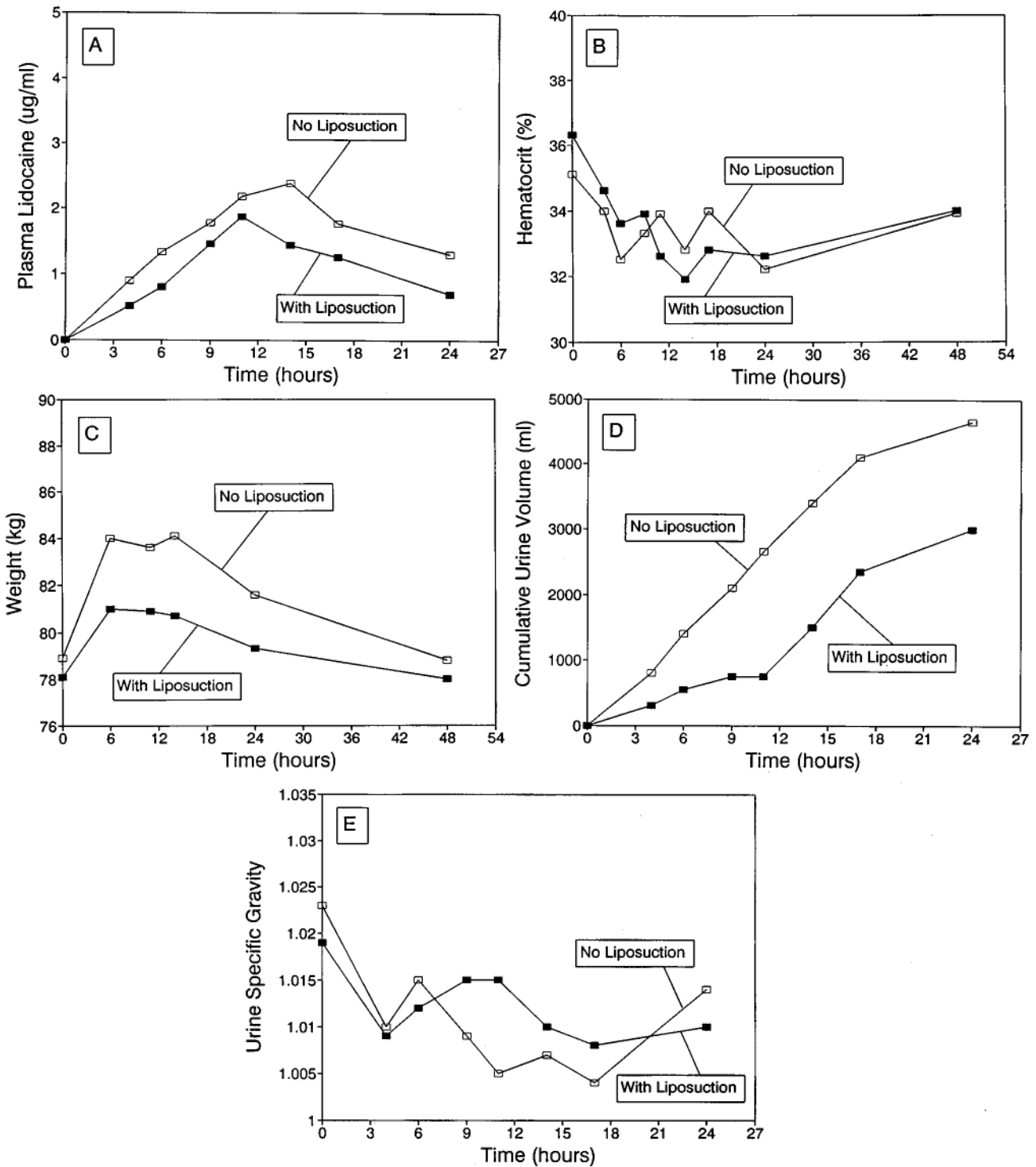


FIG. 3. Comparing the effects of the subcutaneous infiltration of 2625 mg of lidocaine (35 mg/kg) in 5.25 liters of anesthetic solution in a 75-kg woman using the tumescent technique both with no liposuction and with liposuction. The time-dependent changes of (above, left) plasma lidocaine levels, (above, right) hematocrit, (center, left) weight, (center, right) cumulative urine volume, and (below) urine specific gravity were recorded following simple infiltration with no liposuction; then 25 days later, an identical infiltration was followed by liposuction of 1550 ml of supranatant fat, and the measurements were repeated.

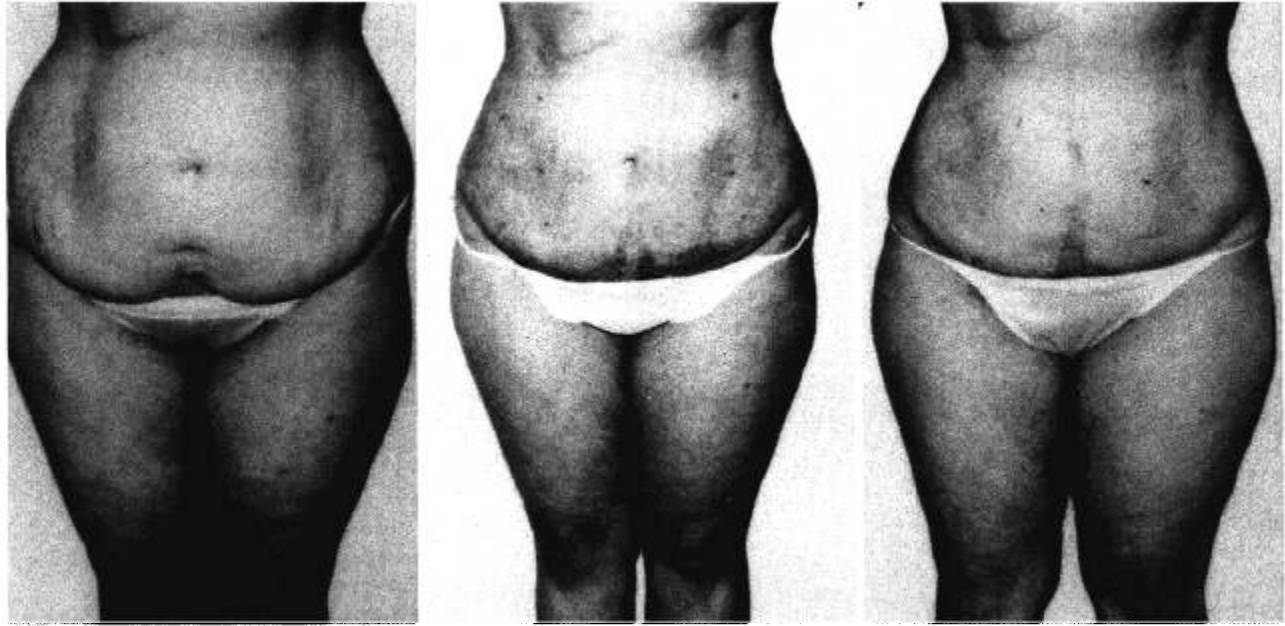


FIG. 4. Three photographs of a 58-kg patient taken before, 1 week after, and 1 month after liposuction by the tumescent technique which removed 22.8 ml of whole blood and 2100 ml of supranatant fat from the abdomen, hips, and waist. Note the minimal bruising 1 week postoperatively. In some patients, liposuction can obviate the need for abdominoplasty and dermolipectomy.

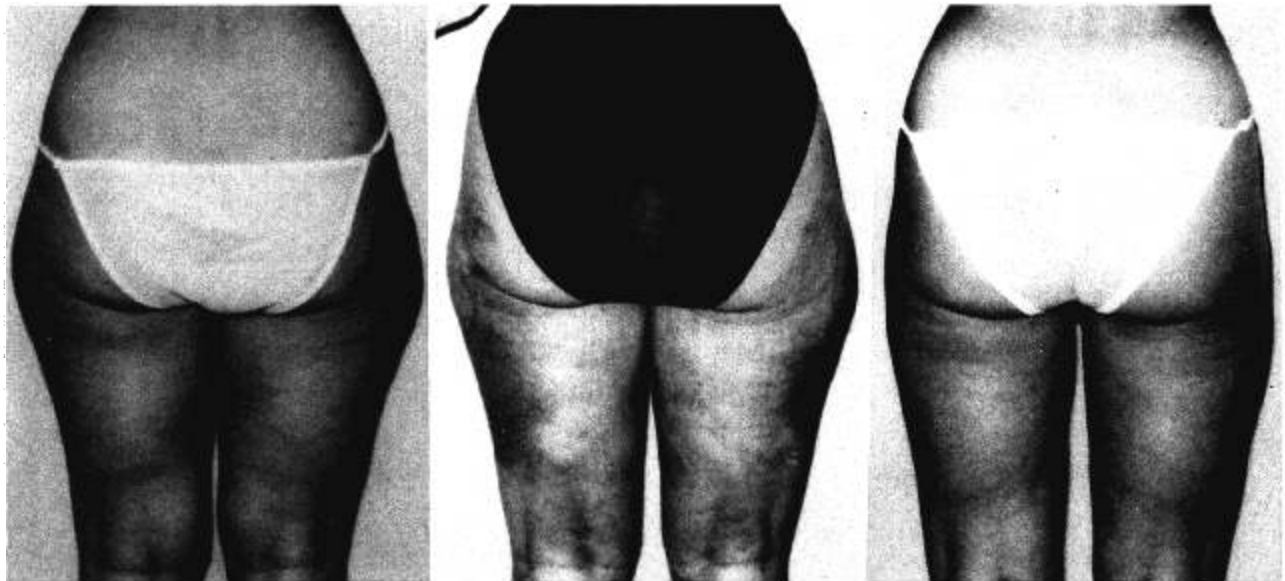


FIG. 5. Three photographs of a 56-kg patient before, 1 week after, and 4 months after liposuction of 20.1 ml of whole blood and 2100 ml of supranatant fat from the outer thighs, anterior thighs, medial thighs, and knees using the tumescent technique. Note the minimal postoperative bruising.

aspirate is blood.³⁴⁻³⁹ In one study of the wet technique, half the patients who had 2500 ml or more of aspirate required hospitalization because of a tendency to develop hypotension.³⁶

The tumescent technique uses the greatest volume of vasoconstrictive subcutaneous infiltration and produces the greatest degree of hemostasis. Using the tumescent technique, less

than 1 percent of the suctioned material is whole blood, and most patients lose more blood during routine preoperative laboratory studies than during large-volume liposuction. The unique aspect of the tumescent technique is that it is the only technique that permits large-volume liposuction totally by local anesthesia without sedation or narcotic analgesics.

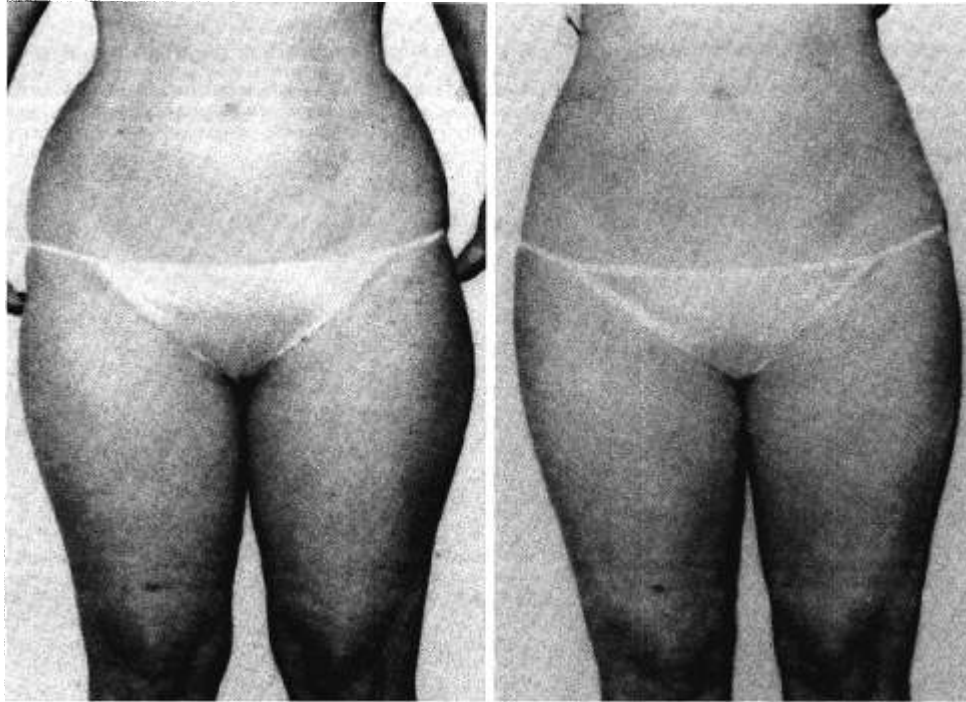


FIG. 6. Preoperative and 3-month postoperative photographs of a 72-kg patient who had 21.7 ml of whole blood removed during liposuction totally by local anesthesia using the tumescent technique without sedation. A total of 2800 ml of supranatant fat was removed from the hips, inner and outer thighs, and knees.

Intravascular Fluid Status

In none of the 112 large-volume liposuction patients was there any clinical evidence of intravascular volume depletion despite minimal IV infusion (mean 429 ml) of physiologic saline. Preoperative urine specific gravity was generally greater than postoperative values. Perioperative urine output was greater than 70 ml/h, the traditional textbook normal hourly urine output.⁴⁰ Similarly, the differences between supine and standing postoperative pulse and blood pressure were unremarkable. Plasma volume depletion is indicated by significant changes in blood pressure and pulse rate.⁴¹

The hemodilution and the urine dilution that occurred in the second study are consistent with the finding that there was no clinical evidence of the intravascular fluid depletion with the tumescent technique for large-volume liposuction. The injection of large volumes of fluid into subcutaneous tissues for hydration, known as *hypodermoclysis*, delivers fluids to the exact site where tissue injury will be induced by liposuction. It is an efficient method of preventing third spacing at the site of injury and intravascular fluid deficits (Table III).

Safety of Local versus General Anesthesia

General anesthesia is more dangerous than local anesthesia.^{42,43} Many of the deaths associated with general anesthesia, having occurred in healthy young patients, are the result of human error and are considered preventable.^{44,45} Deaths due to anesthesia are believed to occur at least once in every 2500 to 10,000 administrations of general anesthesia.⁴⁶⁻⁴⁸ The anesthetic agents fentanyl, halothane, and isoflurane are independent predictors of severe outcome, including death.⁴⁹ Life-threatening complications of general anesthesia are the most dangerous aspects of liposuction surgery. In one study of 2009 healthy liposuction patients, complications included a cardiac arrest in a 28-year-old, anaphylactic shock in a 36-year-old, and respiratory arrest in a 49-year-old.¹ Cardiac arrest, lack of sufficient oxygenation of the brain, pulmonary thromboembolisms, and malignant hyperthermia are well-known fatal complications of general anesthesia.^{45,50-54} The high-risk drugs associated with general anesthesia need not be used with the tumescent technique.

Complications are fewer and less catastrophic with local anesthesia than with general anesthe-

PLASMA LIDOCAINE LEVELS OVER TIME

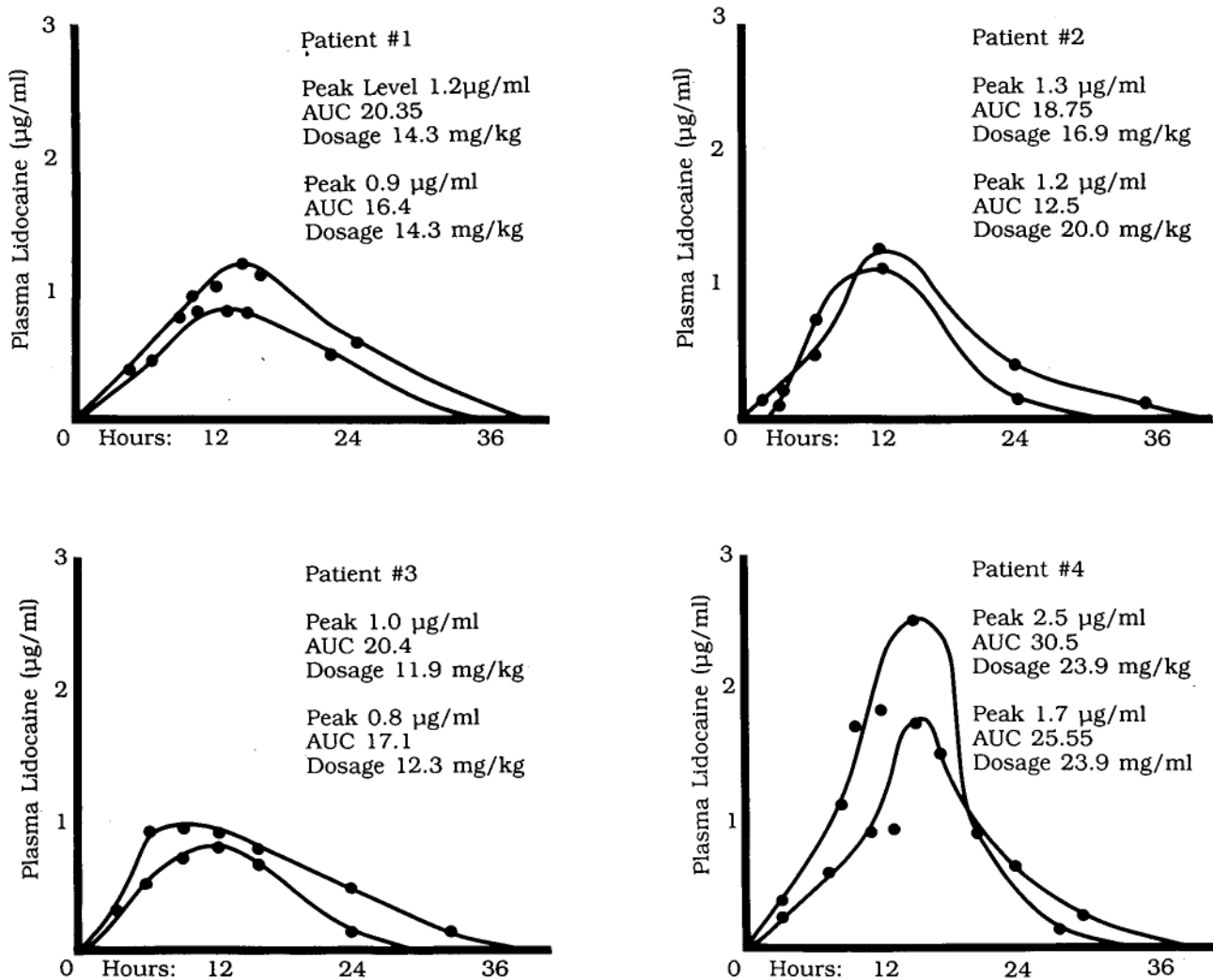


FIG. 7. Lidocaine absorption is not dramatically altered by liposuction. The area under the curve (AUC) of each graph represents the total amount of lidocaine that was absorbed systemically following infiltration into subcutaneous fat using the tumescent technique. In each case, the curve with the larger AUC represents lidocaine absorption as a function of time without liposuction following the infiltration. The curve with the smaller AUC documents lidocaine absorption when liposuction was performed immediately after completing the infiltration. Liposuction reduced both the average amount of lidocaine absorbed systemically and the peak plasma lidocaine concentrations to a similar degree. (Reprinted by permission of the publisher from Klein, J. A. Tumescent technique for regional anesthesia permits lidocaine doses of 35 mg/kg for liposuction. *J. Dermatol. Surg. Oncol.* 16: 254, 1990; copyright by Elsevier Science Publishing Co., Inc.)

sia.⁴³ For example, regional anesthesia is associated with a lower incidence of postoperative thromboembolism.⁵⁵ There is a reduction of intraoperative blood loss with the use of regional anesthesia for colon, gynecologic, hip, and prostate surgery.⁵⁶ In a study of dental anesthetic mortality in England from 1970 to 1979, general anesthesia was associated with 110 deaths, compared with only 10 deaths associated with local anesthesia.⁴³ This difference is all the more remarkable because local anesthetics were used

far more frequently than general anesthesia.

When nitrous oxide, benzodiazepams, and narcotic analgesics are given in doses sufficient to potentially cause respiratory depression, they are general anesthetics.⁵⁷

What Is a Safe Lidocaine Dose?

The Xylocaine (lidocaine hydrochloride) package insert and the 1992 *Physicians' Desk Reference* state, "For normal healthy adults, the individual maximum safe dose of lidocaine HCl

with epinephrine should not exceed 7 mg/kg of body weight and in general it is recommended that the maximum total dose not exceed 500 mg.⁵⁸

Neither the initial manufacturer of lidocaine, Astra Pharmaceutical Products, Inc., nor the United States Food and Drug Administration (FDA) has any data to support this standard dose limitation.⁵⁹ In its 1948 application to the FDA for permission to market lidocaine, the manufacturer simply stated that the maximum safe dose of lidocaine is "probably the same as for procaine."⁶⁰

The widely accepted lidocaine dose limitation of 7 mg/kg is appropriate when commercially available lidocaine (1% or 2%) with epinephrine is infiltrated rapidly or into highly vascular tissue. However, much higher doses are clearly quite safe when more dilute lidocaine (0.05% or 0.1%) with epinephrine is infiltrated over a greater time interval into relatively avascular subcutaneous fat.^{3,16,17} Although 35 mg/kg of lidocaine is the current estimate for a safe maximum lidocaine dose for liposuction by the tumescent technique, doses as high as 52 mg/kg were used in this study without adverse clinical effects. Because there is no well-documented study showing that plasma lidocaine levels are safe with doses greater than 35 mg/kg, caution is necessary when this threshold is exceeded.

Local Anesthetic Toxicity

Lidocaine is the drug of choice for liposuction by local anesthesia. Longer-acting anesthetics have a much greater potential for serious toxicity than lidocaine.⁶¹⁻⁶⁶ Because the anesthetic effects of lidocaine infiltrated into subcutaneous fat by the tumescent technique last for many hours, there is little clinical justification for using longer-acting and potentially more cardiotoxic local anesthetics such as bupivacaine.

The toxicity of a local anesthetic is a function of its peak plasma concentration (Table IV). Peak plasma concentration depends as much on its rate of systemic absorption as on its total milligram per kilogram dose.⁶⁷ The rapid infiltration of 2500 mg of lidocaine for a face lift can be fatal.⁶⁸ When given intravenously, 20 mg/kg of lidocaine can produce cardiovascular collapse and generalized convulsions.⁶⁹ Doses of 35 mg/kg of lidocaine given by the tumescent technique are safe because systemic absorption occurs over 18 to 36 hours.³

TABLE III
Typical Range of Volumes of Dilute Anesthetic Solutions Used with the Tumescent Technique for Infiltration into Various Areas

Abdomen, upper and lower	800-2000 ml
Hip (flank, or love handle), each side	400-1000 ml
Lateral thigh, each side	500-1200 ml
Anterior thigh, each side	600-1200 ml
Proximal medial thigh, each side	250-700 ml
Knee	200-500 ml
Male breast, each side	300-800 ml
Submental chin	100-200 ml

TABLE IV
Plasma Lidocaine Concentration and Toxicity

3-6 µg/ml	Subjective pharmacologic effects
5-9 µg/ml	Objective toxicity
8-12 µg/ml	Seizures, cardiac depression
12 µg/ml	Coma
20 µg/ml	Respiratory arrest
26 µg/ml	Cardiac arrest

Lidocaine Pharmacokinetics

Factors that determine the rate of systemic absorption of a local anesthetic include the drug's concentration, the vascularity of the site of injection, the concomitant use of a vasoconstrictive drug such as epinephrine, and the rate of infiltration.⁷⁰

When plasma lidocaine concentration is plotted as a function of the time after injection, the area under the curve corresponds to the total amount of drug that is absorbed systemically. When a given dose of lidocaine is absorbed rapidly, the peak plasma concentration will be quite high. When an identical dose is absorbed much more slowly, such as when the tumescent technique is used, then the areas under the curves are equal but the peak plasma concentration is significantly lower.⁷¹ The safety of these large doses of lidocaine is not the result of removing lidocaine from the body by aspiration, as has been previously assumed^{72,73} (Fig. 7).

Several recent studies on liposuction have assumed that peak plasma lidocaine concentrations occur within 90 minutes of the infiltration.^{17,74,75} These assumptions were based on previously published data on lidocaine absorption following subcutaneous infiltration⁷⁶⁻⁸³ or intramuscular injection or for nerve block injection,⁸⁴⁻⁹¹ where the peak plasma concentrations occurred within 60 to 90 minutes.

Dilution of lidocaine in a solution containing epinephrine slows its rate of absorption and diminishes its toxicity.⁹² On two separate occa-

sions 1000 mg of lidocaine at different concentrations, 1% lidocaine with epinephrine 1:100,000 and 0.1% lidocaine with epinephrine 1:1 million, were injected slowly into subcutaneous fat over a 45-minute interval with peak lidocaine concentrations of 1.5 and 1.2 $\mu\text{g}/\text{ml}$ occurring at 10 and 14 hours, respectively.³

A slow rate of infiltration of lidocaine with epinephrine delays systemic absorption and diminishes peak plasma lidocaine concentration.⁹³ When approximately 1 gm of lidocaine (0.5% or 1%) with epinephrine (1:100,000) was infiltrated in less than 5 minutes into subcutaneous fat, potentially toxic plasma lidocaine concentrations greater than 5 $\mu\text{g}/\text{ml}$ were attained within 15 minutes.^{94,95} When similar amounts and concentrations were infiltrated slowly over 45 minutes, the peak lidocaine concentration of 1.5 $\mu\text{g}/\text{ml}$ was reached 10 hours after beginning the infiltration.³

Reduced Pain

With good technique, liposuction by local anesthesia is essentially painless. Because the local anesthetic remains in the affected tissues for over 12 hours after the surgery, there is no immediate postoperative pain. The only postoperative analgesia used is acetaminophen. Virtually every one of my patients who has had liposuction by another surgeon under general anesthesia and then has had liposuction by the tumescent technique has found the latter experience to be far less painful.

Formulation of Anesthetic Solution

There is no canonical formulation of the local anesthetic for the tumescent technique. The recipe should be variable depending on the clinical situation. A number of factors determine the minimal sufficient concentration of lidocaine. By exposing sufficient lengths of sensory axons to minimal blocking concentrations of lidocaine, the tumescent technique can anesthetize large volumes of subcutaneous fat.⁹⁶ Current recommendations for formulation of the anesthetic solution for liposuction by the tumescent technique are listed in Table I.

The greater the amount of fibrous tissue in fat and the greater the diameter of the liposuction cannula, the greater is the degree of discomfort associated with liposuction by local anesthesia. For liposuction of fibrous areas such as the abdomen, male flanks, and breasts, the 0.1% concentration is preferred. A cannula greater than 4

mm in diameter may necessitate using higher lidocaine concentrations or using narcotics or general anesthesia.

Although this has not been proven clinically, lidocaine may reduce the risk of infection because it is bactericidal for many pathogens commonly found on the skin.⁹⁷ Lidocaine might improve wound healing by reducing release of tissue-toxic substances from leukocytes such as oxygen free radicals and lysozymes.⁹⁸

The vasoconstrictive effects of epinephrine prolongs anesthesia.⁹⁹ An epinephrine concentration of 1:1 million (1 mg/liter) provides exquisite hemostasis in subcutaneous fat. Tachycardia is unusual except in patients who either receive epinephrine doses greater than 0.035 mg/kg or are unusually sensitive to epinephrine. Clinical experience has shown that 0.5 mg/liter (1:2 million) approaches the minimal effective epinephrine concentration.

Sodium bicarbonate (NaHCO_3), by neutralizing the pH of the anesthetic solution, decreases the burning pain upon infiltration.¹⁰⁰⁻¹⁰² The acidity of commercially available lidocaine causes pain upon subcutaneous infiltration.¹⁰³

Triamcinolone acetonide, at 10 mg/liter of solution, seems to decrease the postoperative soreness experienced by patients. The risks and benefits of dilute triamcinolone are currently the subject of a clinical trial.

In order to avoid the patient feeling chilled, the IV bags of physiologic saline are stored in a blanket warmer at 40°C and removed just before the anesthetic solution is mixed. Using chilled saline or cryoanesthesia does not provide better vasoconstriction but does cause the patient unnecessary discomfort and requires monitoring of the patient's core body temperature.

The use of hyaluronidase is not necessary in the local anesthetic solution for the tumescent technique. It may accelerate systemic absorption of lidocaine, increasing the risk of toxicity by increasing the peak plasma lidocaine concentrations.^{104,105}

Benefits of Avoiding IV Sedation

More than 80 deaths have occurred after the use of midazolam, often in combination with narcotic analgesics, all but three having occurred in patients unattended by anesthesia personnel.¹⁰⁶ Employing anesthetic techniques that avoid drugs that cause respiratory depression eliminates one of the most significant risks of anesthesia.¹⁰⁷ With the tumescent technique for

liposuction totally by local anesthesia, it has been my experience that patients usually do better without IV sedation than when IV sedation is used.

In the course of this study it was noticed that patients who had not taken any sedatives often experienced a certain degree of drowsiness. This drowsiness occurred without and with liposuction in the patient described in the second part of the present study. The peak serum lidocaine concentrations were 1.86 and 2.37 $\mu\text{g}/\text{ml}$.

Postoperative Care

With the tumescent technique, patients are discharged ambulatory 30 minutes after the liposuction procedure is completed. If only one area has been treated, some patients are permitted to drive themselves home.

Because of residual local anesthesia, patients experience no significant soreness for the first 10 to 16 hours after surgery. Although patients do not require postoperative analgesia, acetaminophen is recommended (1000 mg four times daily) because of its anti-inflammatory effects on postoperative trauma.^{108,109}

Patients are encouraged to go for a walk the evening of surgery. There is no postoperative restriction on physical activity; normal exercise may be resumed as soon as it is tolerated. Virtually every patient can return to work at a desk-type job 48 hours after liposuction surgery by the tumescent technique.

CONCLUSIONS

The tumescent technique permits large-volume liposuction totally by local anesthesia. The advantages of using tumescent local anesthesia rather than general anesthesia for liposuction surgery include virtual elimination of surgical blood loss, elimination of the dangers of general anesthesia, elimination of heavy IV sedation, elimination of narcotic analgesics, quicker recovery, and improved aesthetic results.

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REFERENCES

- Dillerud, E. Suction lipoplasty: A report on complications, undesired results, and patient satisfaction based on 3511 procedures. *Plast. Reconstr. Surg.* 88: 239, 1991.
- Courtiss, E. H., Choucair, R. J., and Donelan, M. B. Large-volume suction lipectomy: An analysis of 108 patients. *Plast. Reconstr. Surg.* 89: 1068, 1992.
- Klein, J. A. Tumescent technique for regional anesthesia permits lidocaine doses of 35 mg/kg for liposuction. *J. Dermatol. Surg. Oncol.* 16: 248, 1990.
- Klein, J. A. Tumescent Liposuction: Totally by Local Anesthesia. In G. P. Lask and R. L. Moy (Eds.), *Principles and Practice of Dermatological Surgery*. New York: McGraw-Hill, 1993.
- Adiepon-Yamoah, K. K., and Prescott, L. F. Gas-liquid chromatographic estimation of lignocaine, ethylglycylxylidide, glycylxylidide, and 4-hydroxyxylidine in plasma and urine. *J. Pharm. Pharmacol.* 26: 889, 1974.
- Repogle, S. L. The "standard technique" of liposuction: Viewpoint from a plastic surgeon. *Dermatol. Clin.* 8: 451, 1990.
- Field, L. M. The Dermatologic Surgeon and Liposculpturing. In P. F. Fournier (Ed.), *Liposculpture: The Syringe Technique*. Paris: Arnette Blackwell, 1991. Pp. 265-266.
- Coleman, W. P., III. The history of dermatologic liposuction. *Dermatol. Clin.* 8: 381, 1990.
- Narins, R. S. Liposuction and anesthesia. *Dermatol. Clin.* 8: 421, 1990.
- Klein, J. A. The tumescent technique: Anesthesia and modified liposuction technique. *Dermatol. Clin.* 8: 425, 1990.
- Lillis, P. J. The tumescent technique for liposuction surgery. *Dermatol. Clin.* 8: 439, 1990.
- Stegman, S. J. Technique variations in liposuction surgery. *Dermatol. Clin.* 8: 457, 1990.
- Hanke, C. W., Lee, M. W., and Bernstein, G. The safety of dermatologic liposuction surgery. *Dermatol. Clin.* 8: 563, 1990.
- Lillis, P. J. Liposuction surgery under local anesthesia: Limited blood loss and minimal lidocaine absorption. *J. Dermatol. Surg. Oncol.* 14: 1145, 1988.
- Klein, J. A. Anesthesia for Dermatologic Cosmetic Surgery. In W. P. Coleman, C. W. Hanke, T. H. Alt, and S. Asken (Eds.), *Cosmetic Surgery of the Skin: Principles and Techniques*. Philadelphia: B. C. Decker, 1991. Pp. 39-45.
- Lillis, P. J., and Coleman, W. P., III (Eds.). Liposuction. *Dermatol. Clin.* 8: 381, 1990.
- Klein, J. A. The tumescent technique for liposuction surgery. *Am. J. Cosmetic Surg.* 4: 263, 1987.
- Klein, J. A. Anesthesia for liposuction in dermatologic surgery. *J. Dermatol. Surg. Oncol.* 14: 1124, 1988.
- Mladick, R. A. (Ed.). *Lipoplasty. Clin. Plast. Surg.* 16: 1, 1989.
- Hetter, G. P. (Ed.). *Lipoplasty: The Theory and Practice of Blunt Suction Lipectomy*. Boston: Little, Brown, 1990. Pp. 1-448.
- Teimourian, B., and Rogers, W. B., III. A national survey of complications associated with suction lipectomy: A comparative study. *Plast. Reconstr. Surg.* 84: 628, 1989.
- Mladick, R. A. (Ed.). *Lipoplasty. Clin. Plast. Surg.* 16: 1, 1989.
- Braunstein, M. C. Anesthesia. In G. P. Hetter (Ed.), *Lipoplasty: The Theory and Practice of Blunt Suction Lipectomy*. Boston: Little, Brown, 1990. Pp. 133-142.
- Rohrich, R. J., and Mathes, S. J. Suction Lipectomy. In M. J. Jurkiewicz, T. J. Krizek, S. J. Mathes, and

- S. Ariyan (Eds.), *Plastic Surgery: Principles and Practice*. St. Louis: Mosby, 1990. P. 1559.
25. Toledo, L. S. My Experience with Syringe Liposculpture in Brazil. In P. F. Fournier (Ed.), *Liposculpture: The Syringe Technique*. Paris: Arnette Blackwell, 1991. Pp. 255-257.
 26. Grazier, F. M. (Ed.). *Atlas of Suction Assisted Lipectomy in Body Sculpture*. New York: Churchill-Livingstone, 1992.
 27. Fournier, P. F. *Liposculpture: The Syringe Technique*. Paris: Arnette Blackwell, 1991. P. 163.
 28. Pitman, G. H. *Operative Planning and Surgical Strategies: Liposuction and Aesthetic Surgery*. St. Louis: Quality Medical Publishing, 1993. P. 46.
 29. Dolsky, R. L., Fetzek, J., and Anderson, R. Evaluation of blood loss during liposuction surgery. *Am. J. Cosmetic Surg.* 4: 257, 1987.
 30. Ersek, R. A. Severe and Mortal Complications. In G. P. Hetter (Ed.), *Lipoplasty: The Theory and Practice of Blunt Suction Lipectomy*, 2d Ed. Boston: Little, Brown, 1990. Pp. 223-225.
 31. Committee on Guidelines of Care. Guidelines of care for liposuction. *J. Am. Acad. Dermatol.* 24: 489, 1991.
 32. Hetter, G. P. Blood and fluid replacement for lipoplasty procedures. *Clin. Plast. Surg.* 16: 245, 1989.
 33. Courtiss, E. H., Kanter, M. A., Kanter, W. R., and Ransil, B. J. The effect of epinephrine on blood loss during suction lipectomy. *Plast. Reconstr. Surg.* 88: 801, 1991.
 34. Goodpasture, J. C., and Bunkis, J. Quantitative analysis of blood and fat in suction lipectomy aspirates. *Plast. Reconstr. Surg.* 78: 765, 1986.
 35. Gargan, T. J., and Courtiss, E. H. The risks of suction lipectomy: Their prevention and treatment. *Clin. Plast. Surg.* 11: 457, 1984.
 36. Clayton, D. N., Clayton, J. N., Lindley, T. S., and Clayton, J. L. Large volume lipoplasty. *Clin. Plast. Surg.* 16: 305, 1989.
 37. Dolsky, R. L. Blood loss during liposuction. *Dermatol. Clin.* 8: 463, 1990.
 38. Hetter, G. P. The Use of Low Concentration Epinephrine. In G. P. Hetter (Ed.), *Lipoplasty: The Theory and Practice of Blunt Suction Lipectomy*, 2d Ed. Boston: Little, Brown, 1990. Pp. 143-145.
 39. Hetter, G. P. Blood and Fluid Replacement. In G. P. Hetter (Ed.), *Lipoplasty: The Theory and Practice of Blunt Suction Lipectomy*, 2d Ed. Boston: Little, Brown, 1990. Pp. 191-195.
 40. Woerlee, G. M. *Common Perioperative Problems and the Anaesthetist*. Boston: Kluwer Academic Press, 1988. P. 350.
 41. Levinsky, N. G. Fluid and Electrolytes. In J. D. Wilson, E. Braunwald, K. J. Isselbacher, et al. (Eds.), *Harrison's Principles of Internal Medicine*, 12th Ed. New York: McGraw-Hill, 1991. P. 280.
 42. Kallar, S. K., Keenan, R. L., and Aghdami, A. Complications of Anesthesia. In L. J. Greenfield (Ed.), *Complications in Surgery and Trauma*, 2d Ed. Philadelphia: Lippincott, 1990. Pp. 231-247.
 43. Coplans, M. P., and Curson, I. Deaths associated with dentistry. *Br. Dent. J.* 153: 357, 1982.
 44. Tinker, J. H., Dull, D. L., Caplan, R. A., Ward, R. J., and Cheney, F. W. Role of monitoring devices in prevention of anesthetic mishaps: A closed claims analysis. *Anesthesiology* 71: 541, 1989.
 45. Taylor, G., Larson, C. P. Jr., and Prestwich, R. Unexpected cardiac arrest during anesthesia and surgery: An environmental study. *J.A.M.A.* 236: 2758, 1976.
 46. Epstein, R. M. Morbidity and mortality from anesthesia: A continuing problem. *Anesthesiology* 49: 388, 1978.
 47. Forrest, J. B., Cahalan, M. K., Rehder, K., et al. Multicenter study of general anesthesia: II. Results. *Anesthesiology* 72: 262, 1990.
 48. Keats, A. S. Anesthesia mortality in perspective. *Anesth. Analg.* 71: 113, 1990.
 49. Forrest, J. B., Rehder, K., Cahalan, M. K., and Goldsmith, C. H. Multicenter study of general anesthesia: III. Predictors of severe perioperative adverse outcomes. *Anesthesiology* 76: 3, 1992.
 50. Keenan, R. L., and Boyan, C. P. Cardiac arrest due to anesthesia: A study of incidence and causes. *J.A.M.A.* 253: 2373, 1985.
 51. Tarhan, S., Moffitt, E. A., Taylor, W. F., et al. Myocardial infarction after general anesthesia. *Anesth. Analg.* 56: 455, 1977.
 52. Whittington, R. M., Robinson, J. S., and Thompson, J. M. Fatal aspiration (Mendelson's) syndrome despite antacids and cricoid pressure. *Lancet* 2: 228, 1979.
 53. Mangano, D. T. Perioperative cardiac morbidity. *Anesthesiology* 72: 153, 1990.
 54. Hamilton, W. K. Unexpected deaths during anesthesia: Wherein lies the cause? *Anesthesiology* 50: 381, 1979.
 55. Modig, J., Borg, T., Karlstrom, G., Maripuu, E., and Sahlstedt, B. Thromboembolism after total hip replacement: Role of epidural and general anesthesia. *Anesth. Analg.* 62: 174, 1983.
 56. Modig, J. Regional anesthesia and blood loss. *Acta Anaesthesiol. Scand. Suppl.* 89: 44, 1988.
 57. Moller, J. T., Wittrup, M., and Johansen, S. H. Hypoxemia in the postanesthesia care unit: An observer study. *Anesthesiology* 73: 890, 1990.
 58. *Physicians' Desk Reference 1992*, 46th Ed. Montvale, N.J.: Medical Economics Data, 1992. Pp. 637-639.
 59. Director of Clinical Research, Astra Pharmaceutical Products, Inc., Westboro, Mass., personal communication.
 60. The U.S. Food and Drug Administration, Rockville, Md., personal communication. (This information was obtained under the Freedom of Information Act.)
 61. Feldman, H. S., Arthur, G. R., and Covina, B. G. Comparative systemic toxicity of convulsant and supraconvulsant doses of ropivacaine, bupivacaine, and lidocaine in the conscious dog. *Anesth. Analg.* 69: 794, 1989.
 62. Morishima, H. O., Pederson, H., Finster, M., et al. Bupivacaine toxicity in pregnant and nonpregnant ewes. *Anesthesiology* 63: 134, 1985.
 63. Moller, R. A., and Covino, B. G. Cardiac electrophysiologic effects of lidocaine and bupivacaine. *Anesth. Analg.* 67: 107, 1988.
 64. Tanz, R. D., Heskett, T., Loehning, R. W., and Fairfax, C. A. Comparative cardiotoxicity of bupivacaine and lidocaine in the isolated perfused mammalian heart. *Anesth. Analg.* 63: 549, 1984.

65. Kasten, G. W. High serum bupivacaine concentrations produce rhythm disturbances similar to Torsades de Pointes in anesthetized dogs. *Reg. Anaesth.* 11: 20, 1986.
66. Chadwick, H. S. Toxicity and resuscitation in lidocaine- and bupivacaine-infused cats. *Anesthesiology* 63: 385, 1985.
67. Rowland, M., and Tozer, T. N. *Clinical Pharmacokinetics: Concepts and Applications*, 2d Ed. Philadelphia: Lea & Febiger, 1989. Pp. 33-48.
68. Sunshine, I., and Fike, W. W. Value of thin-layer chromatography in two fatal cases of intoxication due to lidocaine and mepivacaine. *N. Engl. J. Med.* 271: 487, 1964.
69. Yukioka, H., Hayashi, M., and Fujimori, M. Lidocaine intoxication during general anesthesia (Letter). *Anesth. Analg.* 71: 207, 1990.
70. de Jong, R. H., and Bonin, J. D. Local anesthetics: Injection route alters relative toxicity of bupivacaine. *Anesth. Analg.* 59: 925, 1980.
71. Rowland, M., and Tozer, T. N. *Clinical Pharmacokinetics*, 2d Ed. Philadelphia: Lea & Febiger, 1989. Pp. 35-37.
72. Asken, S. *Liposuction Surgery and Autologous Fat Transplantation*. East Norwalk, Conn.: Appleton & Lange, 1988. P. 63.
73. Illouz, Y. G., and de Villiers, Y. T. *Body Sculpturing by Lipoplasty*. Edinburgh: Churchill Livingstone, 1989. P. 115.
74. Gumucio, C. A., Bennie, J. B., Fernando, B., et al. Plasma lidocaine levels during augmentation mammoplasty and suction-assisted lipectomy. *Plast. Reconstr. Surg.* 84: 624, 1989.
75. Lewis, C. M., and Hepper, T. The use of high-dose lidocaine in wetting solutions for lipoplasty. *Ann. Plast. Surg.* 22: 307, 1989.
76. Scott, D. B., Jebson, P. J., Braid, D. P., Ortengren, B., and Frisch, P. Factors affecting plasma levels of lignocaine and prilocaine. *Br. J. Anaesth.* 44: 1040, 1972.
77. Stoelting, R. K. Plasma lidocaine concentrations following subcutaneous or submucosal epinephrine-lidocaine injection. *Anesth. Analg.* 57: 724, 1978.
78. Schwartz, M. L., Covino, B. G., Narang, R. M., et al. Blood levels of lidocaine following subcutaneous administration prior to cardiac catheterization. *Am. Heart J.* 88: 721, 1974.
79. Kosowsky, B. D., Mufti, S. I., Grewal, G. S., et al. Effect of local lidocaine anesthesia on ventricular escape intervals during permanent pacemaker implantation in patients with complete heart block. *Am. J. Cardiol.* 51: 101, 1983.
80. Nattel, S., Rinkenberger, R. L., Lehrman, L. L., and Zipes, D. P. Therapeutic blood lidocaine concentrations after local anesthesia for cardiac electrophysiologic studies. *N. Engl. J. Med.* 301: 418, 1979.
81. Maloney, J. M., III, Lertora, J. J., Yarbrough, J., and Millikan, L. E. Plasma concentrations of lidocaine during hair transplantation. *J. Dermatol. Surg. Oncol.* 8: 950, 1982.
82. Alfano, S. N., Leicht, M. J., and Skiendzielewski, J. J. Lidocaine toxicity following subcutaneous administration. *Ann. Emerg. Med.* 13: 465, 1984.
83. Eyres, R. L., Kidd, J., Oppenheim, R., and Brown, T. C. K. Local anaesthetic plasma levels in children. *Anaesth. Intensive Care* 6: 243, 1978.
84. Collinsworth, K. A., Kalman, S. M., and Harrison, D. C. The clinical pharmacology of lidocaine as an antiarrhythmic drug. *Circulation* 50: 1217, 1974.
85. Tucker, G. T., Moore, D. C., Bridenbaugh, P. O., et al. Systemic absorption of mepivacaine in commonly used regional block procedures. *Anesthesiology* 37: 277, 1972.
86. Raj, P. P., Rosenblatt, R., Miller, J., et al. Dynamics of local-anesthetic compounds in regional anesthesia. *Anesth. Analg.* 56: 110, 1977.
87. Ecoffey, C., Desparmet, A., Berdeaux, A., et al. Pharmacokinetics of lignocaine in children following caudal anesthesia. *Br. J. Anaesth.* 56: 1399, 1984.
88. Braid, D. P., and Scott, D. B. Dosage of lignocaine in epidural block in relation to toxicity. *Br. J. Anaesth.* 38: 596, 1966.
89. Braid, D. P., and Scott, D. B. The systemic absorption of local analgesic drugs. *Br. J. Anaesth.* 37: 394, 1965.
90. Inoue, R., Suganuma, T., Echizen, H., et al. Plasma concentrations of lidocaine and its principal metabolites during intermittent epidural anesthesia. *Anesthesiology* 63: 304, 1985.
91. Blanco, L. J., Reid, P. R., and King, T. M. Plasma lidocaine levels following paracervical infiltration for aspiration abortion. *Obstet. Gynecol.* 60: 506, 1982.
92. Gordh, T. Xylocain: A new local anesthetic. *Anaesthesia* 4: 4, 1949.
93. Scott, D. B. Evaluation of clinical tolerance of local anaesthetic agents. *Br. J. Anaesth.* 47: 328, 1975.
94. Pivaler, K. Systemic lidocaine absorption during liposuction (Letter). *Plast. Reconstr. Surg.* 80: 643, 1987.
95. Richard Hagert, M.D., Department of Plastic and Reconstructive Surgery, School of Medicine, University of South Carolina, Charleston, S.C., personal communication.
96. Raymond, S. A., Steffensen, S. C., Gugino, L. D., and Strichartz, G. R. The role of length of nerve exposed to local anesthetics in impulse blocking action. *Anesth. Analg.* 68: 563, 1989.
97. Miller, M. A., and Shelly, W. B. Antibacterial properties of lidocaine on bacteria isolated from dermal lesions. *Arch. Dermatol.* 121: 1157, 1985.
98. Eriksson, A. S., Sinclair, R., Cassuto, J., and Thomsen, P. Influence of lidocaine on leukocyte function in the surgical wound. *Anesthesiology* 77: 74, 1992.
99. Myers, R. R., and Heckman, H. M. Effects of local anesthesia on nerve blood flow: Studies using lidocaine with and without epinephrine. *Anesthesiology* 71: 757, 1989.
100. McKay, W., Morris, R., and Mushlin, P. Sodium bicarbonate attenuates pain on skin infiltration with lidocaine, with or without epinephrine. *Anesth. Analg.* 66: 572, 1987.
101. Stewart, J. H., Cole, G. W., and Klein, J. A. Neutralized lidocaine with epinephrine for local anesthesia. *J. Dermatol. Surg. Oncol.* 15: 1081, 1989.
102. Larson, P. O., Raji, G., Swandby, M., et al. Stability of buffered lidocaine and epinephrine used for local anesthesia. *J. Dermatol. Surg. Oncol.* 17: 411, 1991.
103. Stewart, J. H., Chinn, S. E., Cole, G. W., and Klein, J.

- A. Neutralized lidocaine with epinephrine for local anesthesia, part II. *J. Dermatol. Surg. Oncol.* 16: 842, 1990.
104. Pettersson, L. O., and Akerman, B. Influence of hyaluronidase upon local infiltration anaesthesia by lidocaine. *Scand. J. Plast. Reconstr. Surg.* 18: 297, 1984.
105. Adriani, J. The clinical pharmacology of local anesthetics. *Clin. Pharmacol. Ther.* 1: 645, 1960.
106. Bailey, P. L., Pace, N. L., Ashburn, M. A., et al. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. *Anesthesiology* 73: 826, 1990.
107. Stoddart, J. C. Postoperative respiratory failure: An anaesthetic hazard? *Br. J. Anaesth.* 50: 695, 1978.
108. Lokken, P., and Skoglund, L. A. Medical therapy of osteoarthritis of the knee (Letter). *N. Engl. J. Med.* 325: 1805, 1991.
109. Skjelbred, P., Lokken, P., and Skoglund, L. A. Postoperative administration of acetaminophen to reduce swelling and other inflammatory events. *Curr. Ther. Res.* 35: 377, 1984.