The Directorate of Health Sciences Institute

Entitled this study "Dermal Fillers: Risks, Awareness And Reported Complications" has been accepted by thesis committee for the degree of Master of Science in Toxicology.

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ABSTRACT

Sabehaayoun N. Dermal Fillers: Risks, Awareness and Reported Complications.

NEU Toxicology Master Thesis, Lefkoşa-TRNC, 2017

The fountain of youth has been pursued since the beginning of history. Nowadays it took the form of dermal fillers. Despite their high safety margin, they are still considered to be foreign bodies in our system that might cause a myriad of complications, either directly after the injection or even years later. By highlighting the risk factors of fillers and collecting enough data about reported complications, in addition to investigating the public awareness through conducting a survey, we intend to create an informative study that will act as a guide for both, the public and the physicians. Data for previously recorded complications of dermal fillers was collected from 5 clinics in Saida and Beirut-Lebanon during the period of February 9 to April 10, 2017. In addition, a survey was conducted, to investigate the awareness of the public about the different types of dermal fillers and their complications at the same period. A total of 18 serious cases were collected from 5 different clinics in Saida and Beirut. The fillers used were either hyaluronic acid or polymethylmethacrylate (PMMA). The cases varied from simple adverse events such as erythema to more severe complications and serious events as serious as skin necrosis. The survey included 300 females from different age groups and backgrounds. According to the answers submitted, 88% of the participants are aware of the dermal fillers in general, in which 31.7% had actually undergone dermal filler procedures while 63% consider the possibility of undergoing such treatments in the future. In this survey, the percentage of participants who chose fillers treatment and were aware of the material used where only 48.4% were aware of the type of injected filler. The survey showed an almost equal percentages about the public's belief in the safety of the dermal fillers with 51.3% believing that they are safe to be used. Participants from different ages seemed to agree about the personal motives and general public motives that might push them to consider dermal filling. As a result, public should be more informed to gain more awareness regarding this field through studies and articles rather than letting them to be mislead by the improper sources.

Key words: Dermal filler, Filler complications, Collected cases, Public awareness

1. INTRODUCTION

Aesthetic procedures are considered to be an outgrowing industry in the last 3 decades with a special attention given to nonsurgical injection procedures with minimally invasive techniques such as dermal fillers. The use of dermal fillers has been progressively increasing with each year, since the year 2000, for soft tissue augmentation and rejuvenation. According to 2015 Cosmetic Plastic Surgery Statistics from The American Society of Plastic Surgeons (ASPS), the use of dermal fillers use comes in the 2nd place after Botulinum Toxin in cosmetic minimally invasive procedures with 6% increase from the year 2014 and 274% from the year 2000 (Fig.1.1 and Fig.1.2). (ASPS Plastic Surgery Statistics Full Report 2015)

COSMETIC MINIMALLY-INVASIVE PROCEDURES	2015	2014	2000	% CHANGE 2015 vs. 2014	% CHANGE 2015 vs. 2000
Botulinum Toxin Type A (Botox®, Dysport®)***	6,757,198	6,673,608	786,911	1%	759%
Cellulite treatment (Velosmooth®, Endermology)	30,810	29,243	23,952	5%	29%
Chemical peel	1,310,252	1,250,059	1,149,457	5%	14%
Intense Pulsed Light (IPL) treatment	646,592	621,724	*	4%	*
Laser hair removal	1,116,708	1,112,046	735,996	0%	52%
Laser skin resurfacing	569,458	543,731	170,951	5%	233%
Ablative	159,795	152,478	*	5%	*
Non-ablative (Fraxel®, etc.)	409,663	391,253	*	5%	*
Laser treatment of leg veins	207,862	207,790	245,424	0%	-15%
Microdermabrasion	800,340	881,905	868,315	-9%	-8%
Sclerotherapy	322,280	323,609	866,555	0%	-63%
Soft Tissue Fillers	2,440,724	2,295,647	652,885	6%	274%
Calcium hydroxylapatite (Radiesse®)	256,256	257,953	*	-1%	*
Collagen	14,353	16,023	587,615	-10%	-98%
Porcine/bovine-based (Evolence®, Zyderm®, Zyplast®)	14,353	16,023	*	-10%	*
Fat	70,283	67,609	65,270	4%	8%
Hyaluronic acid (Juvederm Ultra®, Juvederm® Ultra Plus®, Perlane®, Restylane®, Belotero®)	1,951,692	1,802,247	*	8%	*
Polylactic acid (Sculptra®)	130,089	134,471	*	-3%	*
Polymethyl-methacrylate microspheres (Artefill®)	18,051	17,344	*	4%	*
TOTAL COSMETIC MINIMALLY-INVASIVE PROCEDURES	14,202,224	13,939,362	5,500,446	2%	158%

Figure 1.1. The American Society of Plastic Surgeons (ASPS) statistics for the progress of cosmetic minimally-invasive procedures.

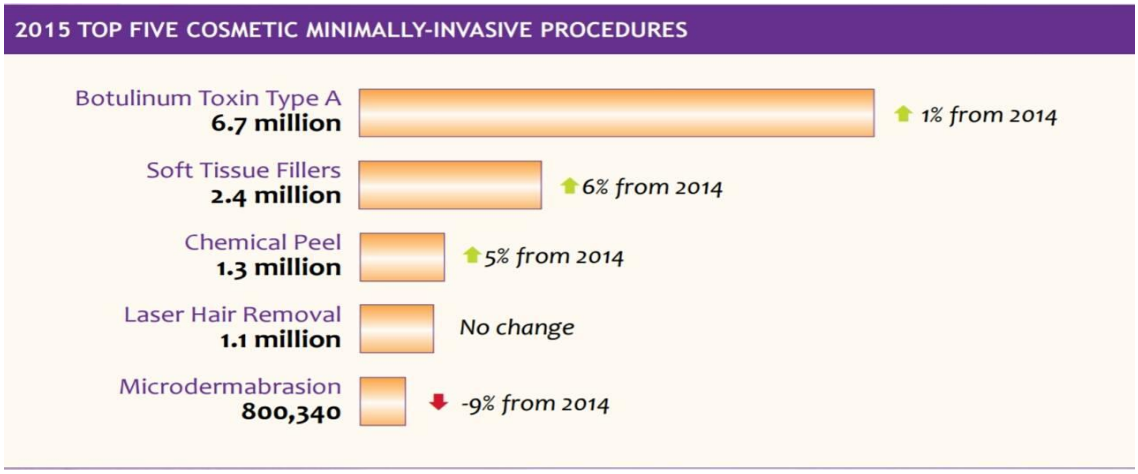

Figure 1.2. 2015 Top Five Female Cosmetic Minimally-Invasive Procedures

These statistics match the data from the American Society for Dermatologic Surgery (ASDS). This enormous increase is logical taking into consideration their ease of application, low cost, significant beneficial effect on appearance, and relatively low rate of complications. We cannot exclude the fact that that the fillers are foreign bodies in our system. As a result, as the indications and the number of procedures performed increase, so do the reports of a myriad of complications both immediately after the injection and potentially months or years later due to various factors.

The aim of this study is to have a well-organized informative reference and data for physicians as well as the public by collecting data about previously recorded dermal filler complications from specialized clinics and investigating the awareness of the public through a survey.

2. OVERVIEW

Dermal fillers are substances injected in the dermis for the sake of soft tissue augmentation to enhance or replace volume that is lost in any part of the skin or subcutaneous fat. Fillers form an effective tool in rejuvenation, either as a stand-alone treatment or in combination with other procedures. Dermal fillers are used for a multitude of applications:

- Wrinkles (fine to deep)
- Facial deformities
- Sunken scars
- HIV-related lipoatrophy in hands, neck and decollete.
- Filling of rhytides and folds
- Volume replacement and enhancement (including cheek and chin augmentation, tear trough correction, nose reshaping, midfacial volumisation, lip enhancement, hand rejuvenation, and the correction of facial asymmetry)

The FDA has NOT approved soft tissue fillers to:

- Increase breast size (breast augmentation)
- Increase size of the buttocks
- Increase fullness of the feet
- Implant into bone, tendon, ligament, or muscle

The FDA has NOT approved liquid silicone or silicone gel for injection to fill wrinkles or augment tissues anywhere in the body.

1. The practice of soft tissue augmentation goes back to the 1800s with Neuber in 1893, who took fat from the arms and transplanted it into facial defects. In 1899, paraffin was used and was later given up due to foreign body granulomas or paraffinomas. In the 1940s and 1950s, silicone was used extensively until the commissioner of the US Food and Drug Administration (USFDA) declared the use of injectable silicone to be illegal. The field of soft tissue augmentation underwent a revolutionary change in the early

1970s when researchers at Stanford University worked on the use of animal and human collagen as implant materials (Fig. 2.1).

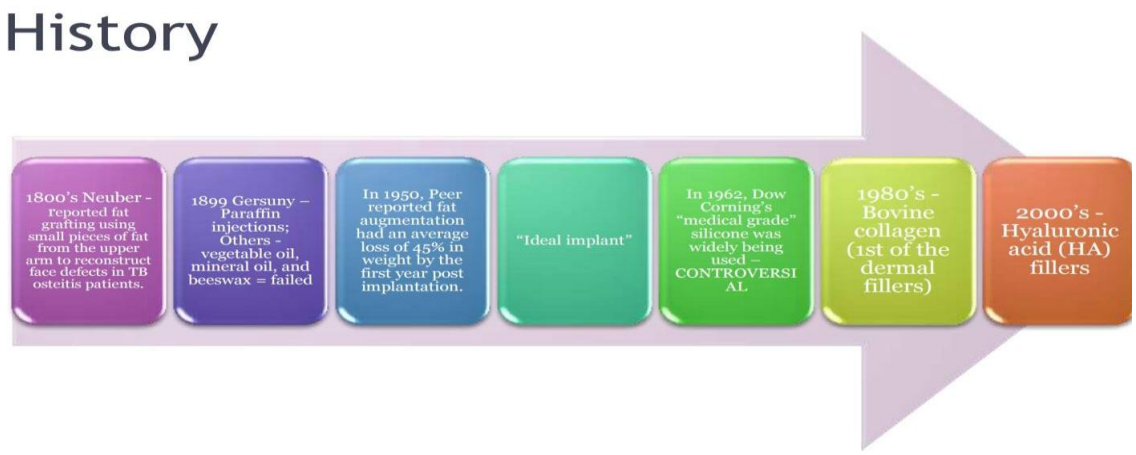

Figure 2.1. History of Dermal Fillers (Edionwe S, 2012)

On 1981, Bovine collagen was approved by FDA for the use of soft tissues injection. Since then, a number of filler materials have been manufactured and approved by the FDA. New fillers merely had to meet or exceed the safety and efficacy standards of collagen products. By 2010, collagen is assumed to be excluded from markets worldwide except for bovine collagen, which is used as a carrier for Polymethylmethacrylate (PMMA) microspheres. As public awareness and acceptance of dermal fillers grows, so does the size of the market, with an estimated 160 products currently available worldwide from more than 50 companies (Bader RS, et al., 2017).

The FDA has approved a variety of different filler materials, each with a distinct composition, injection profile, and duration of effect. Currently, Hyaluronic acid (HA) is the most commonly used injectable, followed by Calcium hydoxyapatite (CaHA), and Poly-L-Lactic acid (PLLA). Success of an implant/filler is predicated upon its proximity to meeting the criteria of an "ideal" implant:

- Biocompatibility
- Minimal inflammation
- Non-immunogenic
- Non-carcinogenic/non-teratogenic

- Biodegradable or easily-retrievable
- Predictable
- Adjustable to the patient's anatomy
- Persistent but not necessarily permanent
- Natural appearance

Expectations of consumers for the product when undergoing such procedures would be:

- Feel natural under the skin
- Take little time to inject
- Be ready to use
- Low risk of complications
- Inexpensive
- Long lasting

3. CATEGORIES OF DERMAL FILLERS

Fillers can be classified based on different criteria: (Funt D, 2013; Vedamurthy M, 2008; Soft Tissue Fillers; FDA, 2017)

-Based on origin

- Autologous which is obtained from own tissue such as dermis, fascia, cartilage, and fat.
- Biological fillers such as Hyaluronic acid and collagen
- Synthetic material which is made using silicone, polymethylmethacrylate (PMMA), Calcium hydroxyapatite, and Poly-L-lactic acid (PLLA) with a relatively long duration or permanent effect

-Based on site of placement:

- Dermal
- Subdermal
- Supraperiosteal

-Most importantly and for the sake of better understanding of complications, based on biodegradable (moderate and long duration) vs non-biodegradable or permanent.

- Moderate duration biodegradable fillers are reabsorbed by the body quite quickly, so their cosmetic effects are relatively short-lived (≤ year) such as Hyaluronic acid (HA) and collagen.
- Long duration biodegradable fillers stimulate the body to produce its own collagen have a longer duration of effect (1-2 years) such as calcium hydroxylapatite (CaHA) and poly-L-lactic acid (PLLA).
- Non-biodegradable or permanent provoke a foreign body reaction that stimulates a fibroblastic deposition of collagen around the nonabsorbable microspheres such as polymethyl methacrylate (PMMA), polyacrylamide hydrogel (PAAG) and polydimethylsiloxane oil (LIS-Silicone).

3.1. Collagen

Collagen is a type of protein that is a major part of skin and other tissues in the body. The idea behind using collagen as a filler was that the decreases amount of collagen is the primary reason behind losing the elasticity of the dermis. Collagen fillers are derived from materials extracted from bovine, porcine, and bioengineered human collagen. (Bader RS, et al., 2017; Soft Tissue Fillers, FDA, 2017)

3.1.1. Bovine Collagen

Bovine collagen was the first FDA-approved dermal filler and was commonly used until 2010. 3 types of bovine collagen were manufactured: Zyderm I, Zyderm II and Zyplast in which all of them contain 95% type I bovine collagen and 5% type III bovine collagen. This type of collagen is different from the human one which will increase the possibility of allergic reactions. For this purpose allergy testing is a must before injection. This test should be done twice prior to the actual injection in which the 1st test is done 6 weeks earlier followed by another test 4 weeks , later. 2 weeks interval should be left between the last test and the actual filling procedure. Allergy testing is performed by injecting 0.1 mL of Zyderm I into the superficial dermis on the anterior forearm. The test areas should be read 48 hours after injection for signs of redness and/or edema, often accompanied by pruritus. (Haneke E, 2015; Bader RS, et al., 2017; Steven H, 2008)

Zyderm I: Is a highly purified collagen made from calfskin with a concentration of 35 mg/mL collagen dispersed in a phosphate-buffered physiological saline containing 0.3% lidocaine. After injection, implant undergoes syneresis, saline is lost, and suspended collagen condenses into a soft cohesive network of fibers; network is responsible for restoring skin contour; implant takes on the texture of normal host tissue and is subject to the same stresses and aging process.

It is used for depressed scars, facial contour enhancement including lips, dermal atrophy from disease or corticosteroid injections and wrinkles, creases, and lines caused by facial expression or aging. The injection is in the form of single-use syringe with 30-gauge needle; pierce skin at a 45° angle into the papillary dermis for superficial rhytides. Because the concentration of collagen is low, overcorrection is needed, which will settle down to full correction within 24-48

hours. Injection into the superficial dermis is recommended. Deeper injection may result in immediate correction, but results are lost more quickly. It lasts from 3 to 6 months and it should not be injected more than 30 mL total in a 1-year period.

Zyderm II: It is same as Zyderm I but with a collagen concentration of 65 mg/mL and it should not be injected more than 15 mL total in a 1-year period. It is more commonly used for acne scars. The higher concentration of collagen makes this dermal filler thicker and less flexible than Zyderm I and Zyplast with longer correction time. Overcorrection is not recommended with this product as the case in Zyderm I due to the high concentration of collagen present in it.

Zyplast: It is Highly purified collagen made from calfskin, with a concentration of 35 mg/mL cross-linked with glutaraldehyde dispersed in a physiological saline containing 0.3% lidocaine. It is injected as single-use syringe with 30-gauge needle by piercing the skin at a 20° angle into reticular dermis for deeper lines, scars, and furrows. As for the indications, method of action and duration, it is the same as Zyderm I and Zyderm II.

3.1.2. Bioengineered human Collagen

Since there was always a risk of hypoallergenic reactions with bovine collagen, scientists and companies were tempted in creating a safer one and came out with bioengineered human collagen. It did not require any testing prior to using. Dermal fibroblasts are harvested from bioengineered human skin and placed into a 3-dimensional mesh. These fibroblasts synthesize collagen and extracellular matrix proteins, which are then used as a dermal filling agent. In March 2003, the FDA approved 3 bioengineered human collagen dermal fillers, CosmoDerm I-II, and CosmoPlast. (Haneke E, 2015; Bader RS, et al., 2017, Steven H, 2008, Soft Tissue Fillers, FDA, 2017)

CosmoDerm I: It is a sterile device with 3.5 mg/mL of human-bioengineered collagen distributed in a phosphate-based saline containing 0.3% lidocaine. It enhances the network of collagen fibers already present in the same manner as the bovine-derived collagen. It is used for depressed scars, facial contour enhancement including lips, dermal atrophy from disease or corticosteroid injections and wrinkles, creases and lines caused by facial expression or aging. It is injected in a single-use syringe into the superficial papillary dermis in the same manner as Zyderm I and Zyderm II. Its effects last for approximately 3-6 months with a limitation of 30 mL over a 1-year period.

CosmoDerm II: It is same as CosmoDerma I but with twice the collagen concentration with same uses but limitations of 15 mL over a 1-year period.

CosmoPlast: It is sterile device composed of highly purified human-based collagen cross-linked with glutaraldehyde and dispersed in a phosphate-buffered physiological saline with 0.3% lidocaine. It is injected in a single-use syringe injected into the mid-to-deep dermis and should not be injected more than 30 mL over a 1-year period. As for the indications, method of action and duration, it is the same as CosmoDerm I and CosmoDerm II.

3.1.3. Porcine collagen

The latest addition to the collagen dermal filler market was a new, naturally occurring collagen filler that is derived from porcine (pig) tendons. Since it matches the human collagen to a high extent, the risk of allergy is remote and no skin testing is required prior to treatment. It is composed of 3.5% (35 mg/mL) homogeneous type I collagen that was extracted and purified from porcine tendons and suspended in phosphate-buffered saline and which has been cross-linked with ribose rather than glutaraldehyde as the previous generations of collagen. After injection, implant undergoes syneresis, saline is lost, and suspended collagen condenses into a soft cohesive network of fibers; network is responsible for restoring skin contour; implant takes on the texture of normal host tissue and is subject to the same stresses and aging process.

It is indicated for the correction of moderate-to-deep facial wrinkles and folds, such as nasolabial folds. It is injected in a half-inch, 27-gauge needle in which depth of injection and quantity administered vary(ideally into the mid-to-deep dermis) using linear threading technique, tunneling technique, serial puncture injections, or combinations to achieve optimal results; supplied in a single-use glass syringe (1 mL). It is effects lasts for approximately 6 months and it should not be injected more than 30 mL total in a 1-year period. (Haneke E, 2015; Bader RS, et al., 2017, Steven H, 2008, Soft Tissue Fillers, FDA, 2017)

3.2. Hyaluronic Acid (HA)

Hyaluronic acid is the most prominent glycosaminoglycan in the skin. It consists of repeating units of the monosaccharide D-glucuronic acid and the amino sugar N-acetyl-D-glucosamine linked together via alternating beta-1,4 and beta-1,3 glycosidic bonds. It is an integral part of the natural extracellular matrix which is found in high amounts in several connective tissues including the skin, the vitreous humor of the eye and the synovial fluid. HA is considered to be the most popular dermal filler to replace volume loss due to normal aging for several reasons

including: its hygroscopic property, biocompatibility, reversibility (degraded by hyaluronidase) and its risk of immunogenicity is low since hyaluronic acid is reportedly identical in all species. Sources of hyaluronic acid used in dermal fillers can be from bacteria or rooster combs (avian).

Properties: HA can be manipulated to enhance its effect through cross-linking their dimers, their degree and method of chain cross-linking, the uniformity and size of their particles, and their concentration. The effect and duration of HA highly depends on the previously mentioned factors. Increased cross-linking and concentration increase the viscosity and elasticity as well as the resistance to degradation by native hyaluronidase. The hydrophilic nature of HA means that the more concentrated and/or large particle products will tend to absorb more water, and thus produce more tissue swelling after injection. Another factor that plays a role in the expected outcomes of HA is the size of their microspheres. HA can be biphasic, contain a range of microsphere sizes, or monophasic, contain homogeneous microspheres and considered to be the preferred HA. The degree of hardness (G') also plays a role in the effect of HA. The different HAs have varying degrees of hardness (G'), which will influence their suitability for a particular procedure. In general, the greater the G' of the product, the deeper it should be injected.

How it works: HA is a major component of the extracellular matrix of the dermis, where it is a major contributor to the formation a resilient gel-like ground substance that resists compressive forces. Due to its water-binding affinity, hyaluronic acid forms a high viscosity hydrated polymer that purportedly maintains much of its volume by binding additional molecules of water as it degrades. Hydrogen bonding occurs between adjacent carboxyl and N-acetyl groups to the extent that it retains up to 1000 times its weight in water. When water is drawn into the HA matrix, it has been shown to create a swelling pressure or turgor that enables the HA complex to withstand compressive forces.

3.2.1. Hyaluronic acid-derived dermal fillers

Over the past several decades, various forms of HA fillers have been developed and approved by the FDA and they differ in many aspects. (AbdulJabbar MH, 2016; Choi WY, 2015, Funt D, 2013; Dayan SH, 2008; Cavallini M, 2013, FDA, Bader RS, et al., 2017)

Restylane®: It is the 1st chemically-modified hyaluronic acid filler approved by the US Food and Drug Administration (FDA) for the correction of moderate to severe wrinkles and skin folds was in December 2003. It is a non-animal stabilized HA that is made from Equine Streptococci bacteria by biofermentation and formulated to a concentration of 20 mg/mL. It is cross-linked

with BDDA; 80% cross-linked with 2% degree of cross-linking. It adds natural volume as it integrates into the dermal tissue then attracts and binds water molecules to help maintain volume. This dermal filler has been used for correction of the nasolabial folds, marionette lines, tear troughs, and glabellar frown lines, in addition to lip enhancement and cheek augmentation. Other clinical uses include correction of the jowls and nasal deformities. It is supplied in a disposable glass syringe; each syringe contains 0.4 mL, 1 mL, or 2 mL gel for injection into mid to deep dermis. It os effect lasts for 6 months and its limit for use is 20 mL/60 kg (130 lb) body mass per year. In 2010, Restylane-L became available, which contains lidocaine to reduce pain upon injection. Restylane® subdivides into Restylane Touch (Fine Lines), Restylane, Perlane, Perlane-L according to difference size of the constituent particle. Perlane is identical to Restylane except that it consists of larger gel particles which makes it suitable for the correction of deeper folds.

Juvederm (Juvederm Ultra/Juvederm Ultra Plus): In 2006, the FDA approved Juvederm, which is also a non animal stabilized hyaluronic dermal filler. It is a non-animal stabilized HA that is made from Equine Streptococci bacteria and formulated to a concentration of 24 mg/mL. It is cross-linked with BDDE; 90% cross-linked with at least 6% (highest 11%) degree of cross-linking with higher hydrophilic properties than Restylane. It is sterile, biodegradable, nonpyrogenic, viscoelastic, clear, colorless homogenized gel implant. It does not require refrigeration or skin tests prior to use. It adds natural volume as it integrates into dermal tissue then attracts and binds water molecules to help maintain volume. It is indicated for depressed scars, molecules to help maintain volume, dermal atrophy from disease or corticosteroid injections, wrinkles, creases, and lines caused by facial expression or aging. One box contains 2 prefilled syringes, each containing 0.8 mL of hyaluronic acid; injected into mid to deep dermis. Its effect lasts for 6-12 months for Juvederm Ultra and 9-12 months for Juvederm Ultra Plus and its limit for use is 20 mL/60 kg (130 lb) body mass per year.

Figure.3.1. Juvederm injection package (https://www.mexicanpharmacy.com.mx/image/cache/data/Juvederm_UltraXC-600x600.jpg)

Hylaform: The FDA has also approved a line of animal-derived hyaluronic acid products: Hylaform Regular, Hylaform Fine and Hylaform Plus. It is 5.5 mg/mL medium-sized particles of hylan B which is sterile, nonpyrogenic, viscoelastic, clear gel implant composed of cross-linked molecules of hyaluronic acid derived from an avian (bird) source with glutaraldehyde vinyl sulfone. It is injected into dermal tissue to provide space-occupying viscoelastic supplement for the extracellular matrix of connective tissue; this viscoelastic supplementation or augmentation of dermal tissue results in temporary correction of skin contour; binds water to skin to enhance volume. It is indicated for depressed scars, facial contour enhancement, including lips, dermal atrophy from disease or corticosteroid injections, wrinkles, creases, and lines caused by facial expression or aging. It is injected into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds and its limit for usage is 20 mL/60 kg (130 lb) body mass per year.

Captique: It is approved by the FDA in 2004. This dermal filler is identical to Hylaform except that it is derived from a bacterial source through fermentation. This dermal filler is slightly stiffer than Hylaform. Captique is stored at room temperature and no skin test is required before use. Its effect lasts for 4 months and the limit for using is 20 mL/60 kg (130 lb) body mass per year.

Prevelle Silk: This dermal filler is a colorless hyaluronic acid gel that was FDA approved for use in 2008 and was the first hyaluronic acid dermal filler to contain lidocaine. It adds natural volume as it integrates into dermal tissue; then, attracts and binds water molecules to help maintain volume. It is indicated for Moderate-to-severe facial lines, folds, and wrinkles. It is injected into mid-to-deep dermis with an effect lasting for approximately 6 months and with the limit of 20 mL/60 kg (130 lb) body mass per year.

Hydrelle (formerly Elevess): It is the newest chemically-modified hyaluronic acid filler to be approved by the FDA in 2009. It is manufactured from equine streptococci and formulated to a concentration of 28 mg/mL and cross-linked with BCDI (novel linker). It is injected into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds).

3.3. Poly-L-Lactic Acid (PLLA)

This novel semi permanent filler (Sculptra) differs from all other agents in several aspects. It was approved by the FDA in 2004 for HIV associated lipoatrophy and 2009 for facial rejuvenation.

Poly-L-lactic acid is a synthetic, biodegradable, biocompatible, immunologically inert peptide polymer from the alpha-hydroxy-acid family.

Particles of poly-L-lactic acid stimulate formation of new collagen (collagen neosynthesis) in the skin, adding volume over time, thus it is a dermal stimulating agent, not a true dermal filling agent. Unlike dermal fillers, results are not appreciated for 4 or more weeks. Lastly, most patients require 2-3 treatment sessions that are at least 4-6 weeks apart. It is supplied as a sterile, freeze-dried preparation for injection in a clear glass vial; to be injected into the deep dermis or subcutaneous layer (even if it is injected subdermally, dermal neocollagenesis occurs). Poly-L-lactic acid must be premixed prior to use, making immediate treatment impossible. The effects of PLLA generally become increasingly apparent over a period of time and its efficacy may last up to 2 years. Volume should be limited to approximately 0.1-0.2 mL per each individual injection; the volume of product injected per treatment area varies depending on surface area to be treated. No skin test is required prior to treatment. The product is stored at room temperature, although it must be reconstituted prior to treatment. (Funt D, 2013; Dayan SH, 2008, Haneke E, 2015; Bader RS, et al., 2017, Soft Tissue Fillers, FDA, 2017)

3.4. Calcium Hydroxylapatite

This novel filler, Radiesse, was FDA approved in December 2006 for the correction of facial wrinkles and folds and for the correction of HIV-associated facial atrophy. In 2009, it received FDA approval for cosmetic use in non-HIV patients as well. In 2010, Radiesse was released, which contains lidocaine to reduce pain upon injection. Calcium hydroxylapatite is a type of mineral that is commonly found in human teeth and bones. It is a sterile, nonpyrogenic, semisolid, cohesive implant whose principal component is synthetic calcium hydroxylapatite (30%) suspended in a gel carrier of sterile water for injection, glycerin, and sodium carboxymethyl-cellulose (70%); Radiesse (1.5 mL, 0.8 mL) has a calcium hydroxylapatite particle size range of 25-45 μ m and should be injected with a 25- to 27-gauge needle.

Like PLLA, it stimulates formation of new collagen (collagenesis) in the skin, adding volume over time, It is indicated for subdermal implantation for restoration or correction of signs of facial fat loss (lipoatrophy) in people with HIV infection; also for subdermal implantation for correction of moderate-to-severe facial wrinkles and folds, such as nasolabial folds. If calcium hydroxylapatite is injected into the too superficial layer, it would appear as a white nodular finding. And normal muscle movement results in filler migration and dislocation especially in

the lip. Eventually, this action causes nodule formation superficially thus it is not recommended for injection to the lip. It is Supplied as 1.5-mL or 0.8-mL syringe; insert needle with bevel down at approximately 30° angle to skin; needle should slide under the dermis to the point where the injection should begin; advance the needle into the subdermis to the starting location; slowly inject material in linear threads, while withdrawing needle, until desired level of correction is achieved. Although the gel carrier is lost by 6 months, causing depreciation of initial results, the effects of this material last approximately 18 months. Amount injected varies depending on site and extent of restoration or augmentation desired. Use a 1:1 correction factor. No overcorrection needed. No skin test is required prior to treatment, and the product is stored at room temperature. (Choi WY, 2015, Funt D, 2013; Dayan SH, 2008, Bader RS, et al., 2017, Soft Tissue Fillers, FDA, 2017, Bass LS, 2010)

3.5. Polymethylmethacrylate (PMMA) With Bovine Collagen

It was FDA approved for the use as permanent dermal filler in October 2006. This dermal filler is biphasic composed of 20% non-resorbable polymethylmethacrylate (PMMA) microspheres, which are 30-50 μ m in diameter, suspended in a water-based carrier gel composed of 3.5% bovine collagen, 92.6% buffered isotonic water, 0.3% lidocaine, 2.7% phosphate buffer, and 0.9% sodium chloride (Figure 3.2). Around 3 weeks after injection, collagen is deposited around the microspheres virtually encapsulating them, thus microspores provide permanent volume for wrinkle correction (Figure 3.3-3.6). It is FDA approved for the use in facial tissue around the mouth (i.e., nasolabial folds), but it is contraindicated for the use of lip augmentation. It is an aseptic product that has an opaque, off-white appearance and is supplied in a sealed tray containing 5 syringes (3 with 0.8 mL, 2 with 0.4 mL); it must be brought to room temperature prior to use, 26-gauge needle is used. Best cosmetic result achieved by moving needle back and forth 2-3 times beneath each skin fold being treated, while maintaining constant pressure throughout implantation procedure. Overcorrection is prohibited because result is considered to be permanent. Safety of injecting more than 3.5 mL per treatment site or 8.9 mL overall is not established.

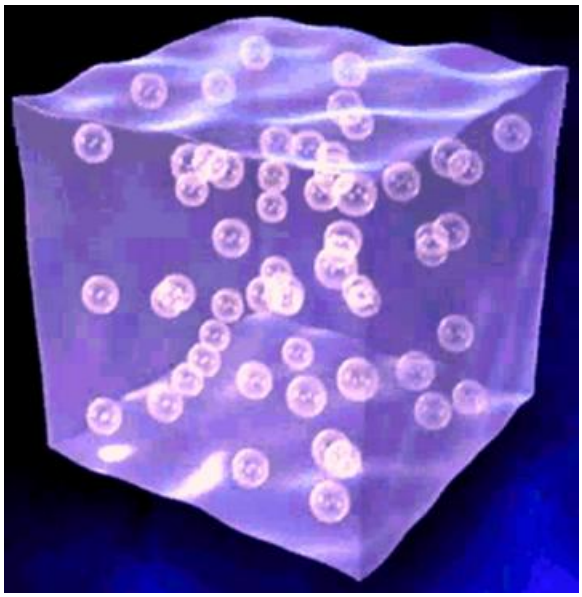

Figure 3.2. ArteFill consists of 20% PMMA microspheres, 30–50 μm in diameter, that are suspended in 80% mostly denatured bovine collage (Lemperle G, 2010)

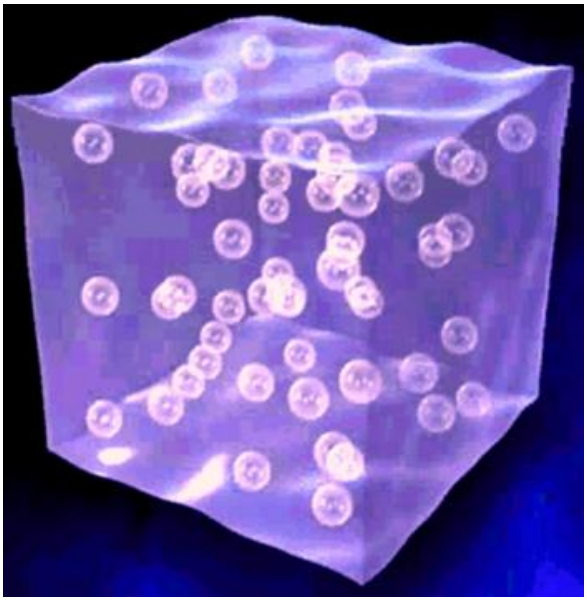

Figure 3.3. For the first few weeks the viscous collagen keeps the microspheres apart to facilitate tissue ingrowth (Lemperle G, 2010)

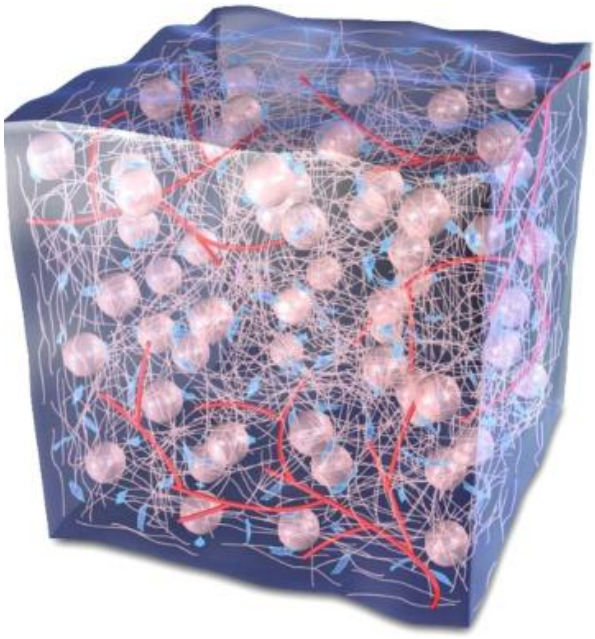

Figure 3.4. At 4 weeks all bovine collagen has been replaced by autologous connective tissue and blood vessels are infiltrating the implant (Lemperle G, 2010)

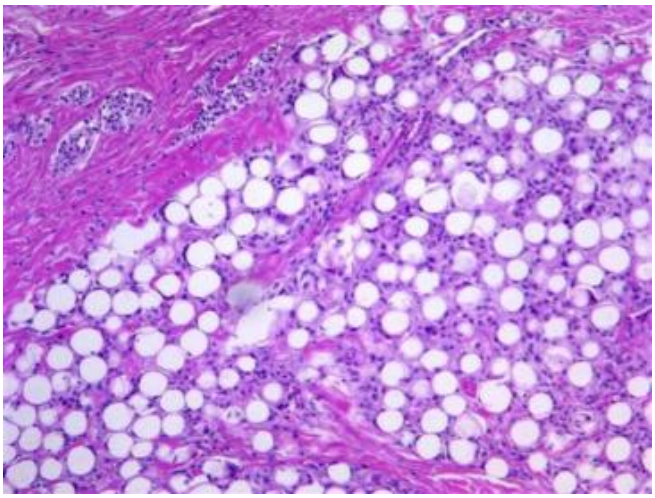

Figure 3.5. At 3 months: capillaries have infiltrated the implant, which has become the patient's own tissue (Lemperle G, 2010)

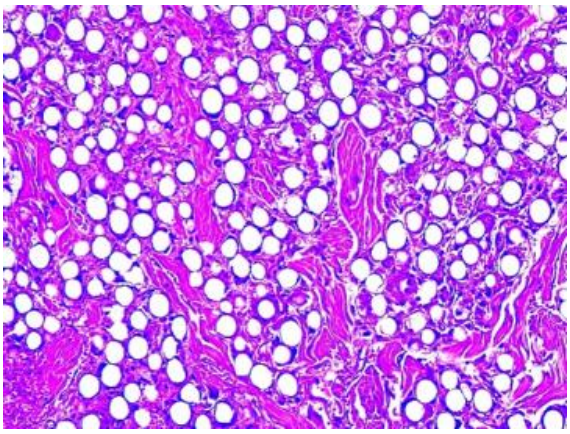

Figure 3.6. Human histology 10 years after Artecoll implantation shows mature connective tissue: active fibroblasts, microencapsulation of each single microsphere, capillary ingrowth, and little foreign body reaction (Lemperle G, 2010)

There is a wide array of PMMA-based injectable products available which have been approved, including PMMA in collagen (Artefill®, Suneva Medical Inc., San Diego, CA, USA), PMMA in carboxyglutamate (Metacrill®, Nutricel, Rio de Janeiro, RJ, Brazil), and PMMA in carboxymethylcellulose (Newplastic®, Lebon Produtos Químicos e Farmacêuticos, Porto Alegre, RS, Brazil). Other hydroxyethylmethacrylate particles suspended in hyaluronic acid (DermaLive®, Dermatech, Paris, France) and polyvinyl hydroxide microspheres suspended in polyacrylamide gel (Evolution®, ProCytech SA, Bordeaux, France), have been withdrawn from the market. (De Jesus, 2015; Choi WY, 2015, Funt D, 2013; Dayan SH, 2008, Bader RS, et al., 2017, Soft Tissue Fillers, FDA, 2017)

Figure.3.7. Artefill Injection set (http://newimagemedicalspas.com/arte-fill/)

4. DERMAL FILLERS COMPLICATIONS AND TREATMENT APPROACHES

The different types of dermal fillers come with different characteristics, associated risks, and injection requirements. Logically speaking, permanent and semi-permanent fillers have potentially more adverse effects than temporary fillers. Although soft-tissue fillers have a very favorable safety profile, they are still considered to be foreign bodies in our system, thus they all have the tendency to cause complications, mostly due to volume injected or techniques used, though some are associated with the material itself. Luckily the majority of these adverse events are mild and transient, but rarely, some of these adverse events can be serious to a big extent. It is noteworthy that most of the complications are avoidable with proper planning and technique.

4.1. Classification of dermal filler complication by onset of adverse event

The adverse events of dermal fillers are divided into early events and delayed events. (Haneke E, 2015; Edwards PC, 2007, Kim JH, 2014)

Early events (occurring up to 1 week after treatment)

-Injections site reactions:

- Erythema
- Edema
- Pain/tenderness
- Bruising
- Itching

-Infection

- Erythema
- Edema
- Pain/tenderness
- Acne papule formation
- Nodule/abscess

-Hypersensitivity

- Erythema
- Edema

- Pain/tenderness
- Non-fluctuant nodules

-Lumps, asymmetries, contour irregularities caused by technique and placement errors

-Skin discoloration

- Redness
- Whiteness
- Hyperpigmentation

-Local tissue necrosis due to vascular occlusion

Delayed events (Occurring weeks to years after post-treatment)

-Infection (atypical e.g. mycobacterial)

- Erythema
- Edema
- Pain/tenderness
- Nodule/abscess
- Systemic response to infection biofilm

-Foreign body granuloma

-Migration of implant material

-Immune reactions (local at site of injection and generalized)

-Persistent discoloration

-Persistent scarring

-Malar edema

4.2. Dermal filler complications and post complication assessment

4.2.1. Bruising

There is always a potential of bruising with all dermal fillers especially after injection into the dermal and immediate subdermal planes using fanning and threading techniques (Figure 4.1).

Bruising is treated with cold compresses after the procedure and vitamin K cream. For persistent staining, treatment with pulsed dye light or potassium titanyl phosphate (KTP) lasers may be effective.

There are some protective procedures to be followed prior to injection to decrease the possibility of bruising. Blood thinning medications should be stopped 1 week in advance. As long as bruising persists, patient should avoid the sun and vigorous exercise so that not to enhance any elevation in blood pressure especially during the 1st 24 hrs. The patient's head should be elevated throughout the procedure and remain so for 24 hours. Bruising can be further limited by use of the smallest gauge needle that can deliver the filler, a slow injection technique with small aliquots of product, use of blunt cannulas, and limiting the number of transcutaneous puncture sites. (Kim JH, 2014, Funt D, 2013, Choi WY, 2015, DeLorenzi C, 2013)

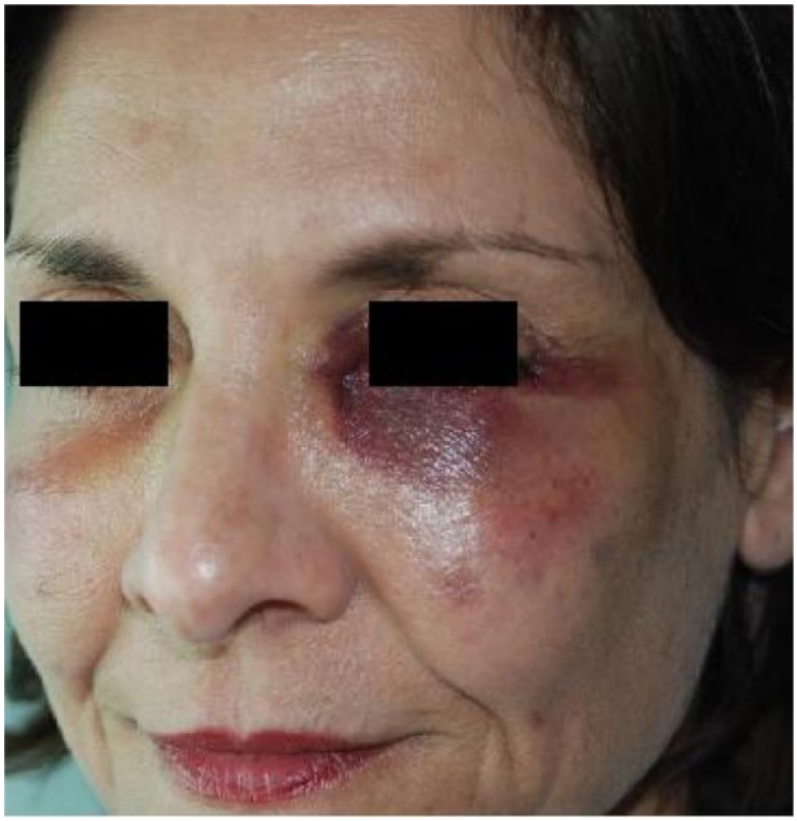

Figure 4.1. Bruising after dermal filler injection (Funt D, 2013)

4.2.2. Edema

Short-term post-traumatic edema: It is perfectly normal to develop some swelling right after injection that resolves by itself within a week maximum. It is mostly related to volume and technique. Cold compression and applying pressure helps to treat the symptoms. (Funt D, 2013; Kim JH, 2014, Bader RS, et al., 2017).

Antibody-mediated edema (angioedema): Angioedema occurs within hours of exposure. Reactions can be severe and can last for several weeks. They can also be unique to injection site or can be more generalized. It is characterized by rapid swelling of deep layers of skin early after injection. Reactions may be acute (<weeks duration) or chronic (≥ 6 weeks duration). In case the acute edema was mild, it is treated with ice or cold compressions. In case the acute edema was severe, or mild edema was persistent, oral or injected antihistamines are used. If this treatment was not responsive, then we should refer to oral or intravenous corticosteroids. In case of chronic edema, the 1st line of defense should be non-sedating antihistamines. If still persistent then the next step would be sedating histamines, if still non responsive, oral corticosteroids and/or immunosupressants would be our last resort. It is difficult to predict but can be avoided to a certain extent by taking the history of the patient. Patients with known allergies to avian or bacterial proteins should not be treated (Fig. 4.2). (Funt D, 2013; Kim JH, 2014, Bader RS, et al., 2017).

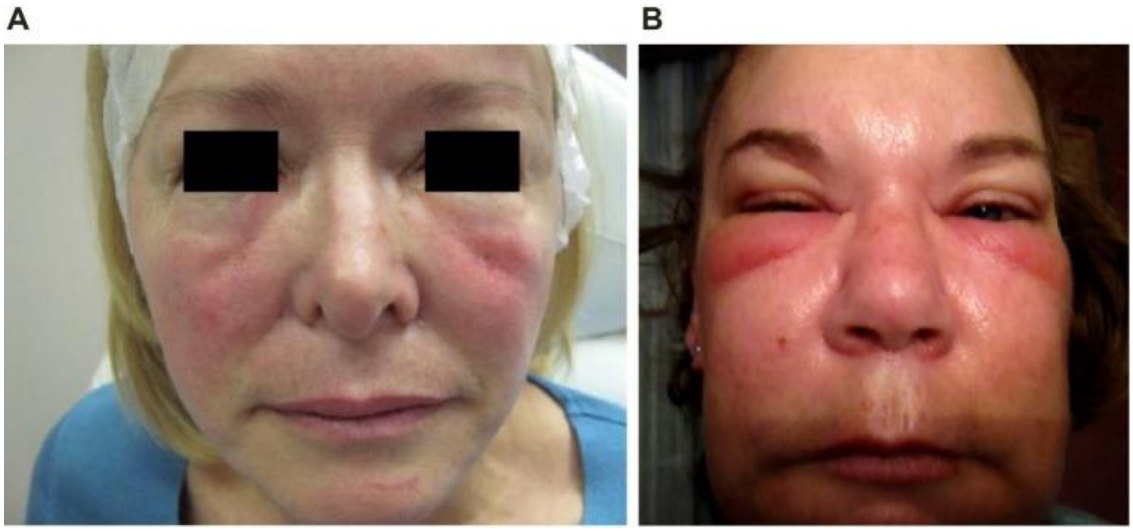

Figure 4.2. Acute generalized facial edema (Funt D, 2013)

Non-antibody mediated (delayed) edema : Delayed hypersensitivity reactions are characterized by induration, erythema, and edema, and are mediated by T lymphocytes rather than antibodies. They typically occur 1 day after injection, but may be seen as late as several weeks after injection and may persist for many months. In case the reaction was due to hyaluronic acid filler and was not responsive to antihistamines, then the allergen should be removed through hyaluronidase, in more than 1 session if needed. If it the filler used was not hyaluronic acid, and the patient was not responsive to antihistamines then symptoms should be controlled with lowest dose possible of oral steroids. If symptoms are still persistent, then allergen should be removed through extrusion, dispersion or break down with laser therapy. It is impossible to predict such kind of reactions unless the patient has had filler reactions in the past. (Funt D, 2013; Kim JH, 2014, Bader RS, et al., 2017).

Malar edema: Malar edema is a serious complication that has been reported with all fillers when injected into the infraorbital hollow and tear troughs. It is characterized by persistent swellings within the confines of the orbicularis oculi becoming evident days to several weeks post-treatment. Injection of fillers superficial to the malar septum may augment the impermeable barrier of the malar septum, further impeding lymphatic drainage and resulting in fluid accumulation and malar edema. Fillers injected superficial or deep to the malar septum may also cause edema by direct pressure on the lymphatics when injection volumes are too large. In addition, as the viscosity or G' of the filler increases, the lifting force also increases, and the lymphatics may be more compressed. Usually this kind of edema is difficult to treat. If it was caused by hyaluronic acid, then it should be removed by hyaluronidase in 1 or more sessions until lymphatic obstruction is removed. For fillers other than hyaluronic acid, initial measures include head elevation with message, followed by night time tapping and day time pressure. Further measures include medrol dose pack, intralesional steroids and eventually, disrupting any nodular material. Avoidance precautions should be taken to reduce the incidence by proper patient filler selection. The patient should be asked about any previous episodes of malar edema. The volume of the filler should be limited. Moreover, the filler should be placed deep to the malar septum at immediate preperiosteal level. The use of an HA when treating the infraorbital hollow is recommended since hyaluronidase may be used to dissolve the material if adverse events occur (Fig.4.3). (Funt D, 2013; Kim JH, 2014, Bader RS, et al., 2017).

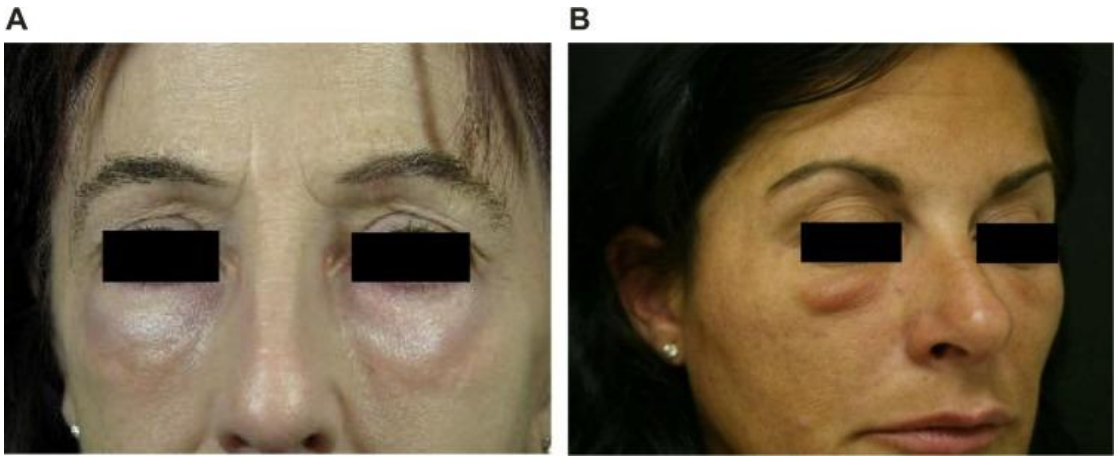

Figure 4.3. Malar edema (Funt D, 2013)

4.2.3. Skin discoloration

Erythema: It's a superficial redness of the skin that is transient right after the injection and is considered to be perfectly normal. If it persists for few days, then it indicates the presence of hypersensitivity reaction. In such case, it is treated as rosacea, using oral tetracycline or isotretinoin. If still persistent then medium length topical steroid is used with the avoidance of long-term use of high-potency steroids not to develop telangiectasia. Lasers are also effective. Vitamin K cream is useful in accelerating resolution of erythema. Patients with rosacea have a higher risk of developing post-injection erythema and should be warned of this prior to beginning the procedure. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013)

Neovascularization: It is characterized by the appearance of new capillaries, arterioles, and venules at the site of dermal filler injection. These tiny vessels can appear days or weeks after the procedure. They are supposed to resolve spontaneously after 3-12 months, but treatment with laser and intense pulsed light (IPL) showed effectiveness in treating telangiectasias. They are caused by tissue trauma as a result of tissue expansion by the product and/or by excessive molding and massage of the product. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013)

Hyperpigmentation: Hyperpigmentation affects different skin types in different manners in which individuals with Fitzpatrick Skin Types IV–VI have higher tendency to develop such reaction after dermal filler treatments. Bleaching agents such as isotretinoin and hydroquinone (2%–8%, in addition to total sunblock creams, are the 1st line of treatment for hyperpigmentation. Chemical peels are also effective in getting rid of resistant hyperpigmentation, If persistent, patient should refer to IPL, a pulsed dye laser or fractional laser. Limiting the number of skin punctures during the injection process by using the linear threading or fanning technique or injecting at the preperiosteal level may reduce post-injection erythema and therefore post-inflammatory hyperpigmentation. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013)

Dyspigmentation: It is characterized by the appearance of a bluish area around the site of injection. It is typically known as the Tyndall effect and it is a result of improper injection of HA in which it is injected into the superficial dermis or epidermis. When HA filler is injected too superficial, a ray of light hits the skin's surface, it is reflected in many different directions, with blue becoming the prominent color that emerges since blue light waves have a higher frequency than red and are more easily scattered. So the more superficial injection of HA filler is, the more bluish it will look and inversely it warns. As soon as this adverse effect is seen, it can be treated with massage and hyaluronidase as an initial step. For HAs that are less susceptible to hyaluronidase because of a high degree of cross-linking or large particle size, multiple treatments may be necessary. As a last resort, dyspigmentation can be treated by nicking the skin with a small-gauge needle (30 gauge) or surgical scalpel (#11 blade) and expressing the superficial, unwanted dermal filler. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013)

4.2.4 Infection

Injecting dermal fillers can lead to infection since it is a procedure that it is breaking the surface of the skin. The infection can be bacterial, viral or fungal. Virulent late infections (biofilms) can also occur. In order to minimize the risk of infection, the patients' history should be taken, including any history of recent dental procedures, any periodontal treatment planned within the next two weeks or any history of chronic sinusitis. The patient should not wear makeup either before or immediately after the procedure. Aseptic technique should be used, including sterilizing the injection site with an effective topical disinfectant, carefully removing the needle

and syringe from sterilized individual packaging, wearing gloves throughout the procedure, and ensuring that the needle is not contaminated during the procedure. Do not wipe excessive filler material from the needle tip with non-sterile gauze; residual amounts of material should be flicked off the needle. It is also important to avoid injecting into inflamed or infected skin, to avoid intraoral injections and to avoid injecting through previous layers of filler. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013; Christensen L, 2013)

Erysipelas and phlegmon: It is a type of in infection that leads to a diffuse inflammation of the skin or connective tissue due to infection. It is a bacterial infection caused by Staphylococcus aureus or Streptococcus pyogenes, unless a new lesion appears 2 weeks after filler treatment, then it is an indication of an atypical infection. If this condition kept untreated, it might lead to sepsis, particularly in elderly people and those with diabetes or other illnesses that alter the immune system. Oral antibiotics with activity against S. aureus, such as cephalexin, dicloxacillin, or nafcillin, are used for treatment. For serious cases, intravenous antibiotics and hospitalization are required. To avoid spreading infection, the area should not be massaged. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013)

Abscess: As mentioned earlier, bacterial inoculations can occur after filler injections as a result of skin surface breakage. Abscess formation is a rare complication occurring any time from 1 week to several years after treatment; it may persist for weeks, and periodically recur for months. When noticed, it should be treated with incision, drainage and antibiotics. Although staphylococci and streptococci bacteria are the most commonly identified organisms, the expressed material should be sent for broad culture for 10–21 days (under aerobic and anaerobic growth conditions). Another approach is to aspirate the lesion with an 18-gauge needle after applying topical anesthesia. The patient should be on empiric broad-spectrum antibiotics immediately, selecting drugs that provide coverage against acid-fast bacilli, atypical mycobacteria, and MRSA, such as macrolide and tetracycline (clarithromycin 500 mg and minocycline 100 mg twice daily for 4–6 weeks). If there is no response after 48-h of follow up, take a 2 mm punch biopsy for tissue culture and adjust the antibiotics accordingly. Hyaluronidase can also be used to dissolve the nidus of the infection in case the used filler was HA. In the case of severe infection, an immunocompromised patient, or infection in facial danger zones (midfacial and periorbital infection can in rare cases result in intracerebral complications), hospitalization is warranted and intravenous antibiotics must be started. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013)

Herpetic Outbreak: Reactivation of herpes simplex infection, especially with lip augmentation, is a very common adverse effect. The majority of herpetic recurrences occur in the perioral area, nasal mucosa, and mucosa of the hard palate. Patients with a history of recurrent herpes simplex outbreaks, certain prophylactic procedures should be taken. It includes treatment with valacyclovir (500 mg twice daily [bid] for 3–5 days) prior to injection and 3 days after. Patients with active lesions of herpes simplex infection should postpone their procedure. Patients who develop new lesions post injection need to be started on an appropriate antiviral regimen and appropriate oral antibiotic if a superadded bacterial infection develops. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013)

4.2.5. Nodular masses

Nodules are common complication for dermal fillers. They are mostly seen in thin skin areas. Nodules must be categorized as inflammatory or noninflammatory.

4.2.5.1. Non-inflammatory nodules

It is a palpable, sometimes visible nodule that appears 2-4 weeks after injection. They form isolated lumps in the area of injection that do not grow, and which are well defined from the surrounding tissue. It happens as a result of over accumulation of the injected filler in the treated area due to poor technique (overcorrection, too superficial placement of a filler), or use of a filler for an incorrect indication such as intramuscular placement in a sphincter muscle. They are divided into early onset and delayed onset. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013)

Early onset: If the nodule was a result of HA filler, hyaluronidase is used. In case of other fillers or the form of HA used had a high level of cross linking that was not resolved by hyaluronidase, the area should be treated with vigorous massage. Nodules that do not resolve may respond to small amounts of intralesional steroids.

Delayed onset: Poor filler placement and the use of particulate fillers (eg, PMMA, CaHA) in highly mobile areas such as the lips can cause delayed-onset non-inflammatory nodules. Treatment follows same steps for early onset nodules. For stubborn ones, begin series of 3 injections of 5-fuorouracil (5-FU), triamcinolone, and lidocaine, or 5-FU and lidocaine. Fractional lasers for eyelids and lips have been reported to improve visible material. Surgical excision would be our last resort.

The incidence of non-inflammatory nodules can be reduced by taking care to avoid too superficial placement of filler, selecting the appropriate filler for the tissue site, massaging after injection to ensure even distribution and smoothness, and avoiding intramuscular injection.

4.2.5.2. Inflammatory nodules

Biofilms: A biofilm is a collection of bacteria surrounded by a protective and adhesive matrix. When a material is injected into the skin or subcutaneous tissue, it can become coated with bacteria and form a biofilm. Biofilms use the implanted filler as a surface on which to attach and excrete their own matrix. This matrix gives them the ability to survive, develop and resist antibiotic treatment. Those bacteria surround themselves with secreted polymers. This excreted polymeric material entraps leukocytes and prevents phagocytosis. These microorganisms develop DNA mutations and achieve subsequent diversity. These bacterial colonies become active when conditions are favorable, for instance after trauma from a further dermal filler procedure, causing a local infection, a systemic infection, or a granulomatous or inflammatory response. These clinical presentations can be manifested at any time after the filler injection that can be as long as years later. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013; Alhede M, 2014)

Practitioner should focus on prevention of biofilm formation since it is difficult to treat such infections. This is why any indurated red area that appears at any time after injection should not be ignored. Culture is not enough to determine the presence of a biofilm, since it is usually negative; this is why we have to refer to fluorescence in situ hybridization for confirmation. The use of scintigraphy with radiolabeled autologous white blood cells is another effective method to diagnose such infections. Broad spectrum antibiotics are our 1st line of defense regardless of the culture results. Antibiotics of choice in this case are quinolones such as ciprofloxacin 500 mg bid and macrolides such as clarithromycin XL 500 mg bid for 4–6 weeks. Using intralesional steroids is out of question not to worsen the case. Removing the filler, whether it is permanent or not, should always be considered to reduce any post-inflammatory potential. If problem is not resolved, then 5-FU injection ≤50 mg/ml (0.5cc) every 4 weeks should be used, combined with steroids if needed. If induration persists after all the previously mentioned procedures, consider laser lysis, and as a last resort, incision and washing out cavity with antibiotics. A persistent nodule with increasing fibroticity that is resistant to antibiotics strongly indicates the [presence

of a foreign body granuloma. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013, Alhede M, 2014)

Although biofilms are not considered to be a common adverse event, it is still beneficial to take some precautionary procedures. The face should be cleansed thoroughly before any filler treatment. Injection through oral or nasal mucosa and injecting hydrophilic permanent materials should be avoided. It is prohibited to inject over previous filler or into traumatized tissue.

Foreign Body Granulomas: As mentioned earlier, a persistent nodule with increasing fibroticity that is resistant to antibiotics strongly indicates the presence of a foreign body granuloma. The purpose of this reaction is to entrap a foreign body in order to prevent its migration when the immune system is unable to degrade it enzymatically or through phagocytosis. The entrapped material usually resists the degradation the and the whole macrophage becomes activated. At this point, it will start secreting cytokines and additional inflammatory products attracting more macrophages. Individual macrophages may become larger (epithelioid histiocytes) or fuse to form multinucleated foreign body giant cells (Fig.4.4). These granulomatous reactions typically have a delayed onset up to years after injection and are clinically described as red papules, plaques or nodules with a firm consistency, sometimes with an irregular and sharp-edged particles indicating increased severity of such reactions. A true granuloma can only be confirmed histologically (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013, Sachdev M, 2010).

Luckily, the occurrence of foreign body granuloma is rare with an incidence of 0.01-0.1%. Our 1st line of treatment would be intralesional corticosteroids such as triamcinolone, betamethasone, or prednisone. In case the filler used was HA then hyaluronidase will be effective. 5-FU will be added to corticosteroids for lesions not responding to steroids alone. This combination has the advantage of reducing the risk of tissue atrophy and telangiectasia due to decreased amount needed of steroids. Surgical excision is the last resort. This adverse event can be avoided with limited filler volume, avoiding intramuscular injections and selecting microspheres with smooth surfaces for use in patients with multiple previous filler procedures (Lee JM, 2015).

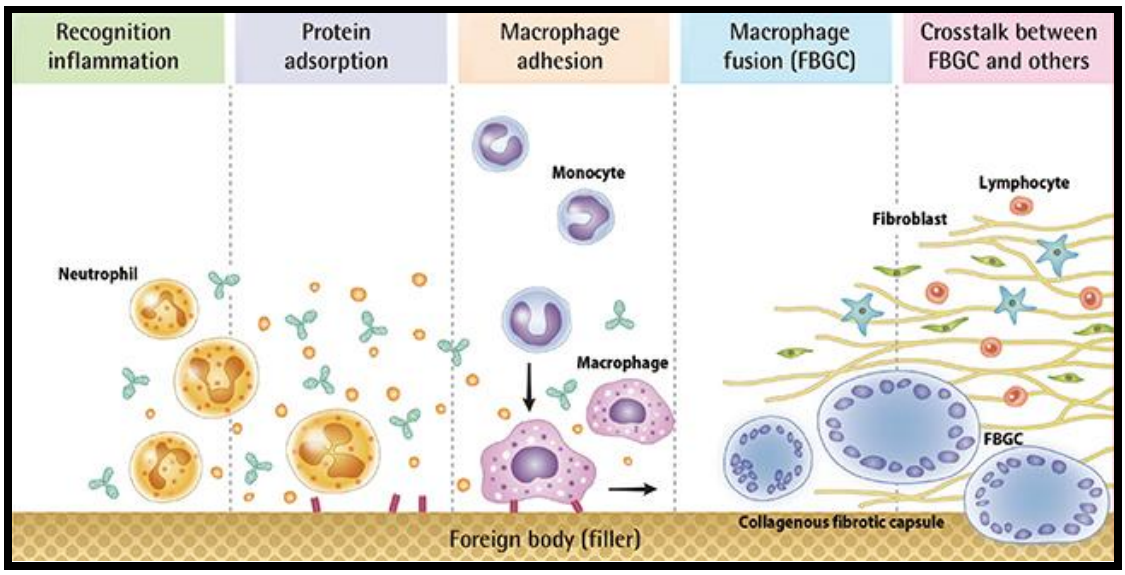

Figure 4.4. Foreign Body Granuloma Formation Phases (Lee JM, 2015)

4.2.6 Paresthesia

Inadvertent or accidental nerve damage is rare but possible complication of dermal fillers that happens as a result of piercing or partially lacerating a nerve by the needle, filler injection into a nerve, compressing a tissue by a product and by excessive molding and massage of product into a nerve foramina. It can be reversible or permanent. The infraorbital nerve is the most susceptible to such injury. It is treated with triamcinolone in small doses, and using lidocaine or saline for disrupting the palpable material. It can be avoided if the practitioner had enough experience and knowledge about the facial anatomy anticipating vital structures. Injecting slowly with a needle in contact with bone prevents intraneural injection (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013).

4.2.7 Vascular occlusion

It is a major immediate most dangerous complication among all dermal fillers. It can be either a localized occlusion, due to intravascular injection interrupting blood glow or over-injecting the filler compressing leading to venous compression and leading to skin necrosis, or distant occlusion due to intra-arterial injection interrupting blood glow or over-injecting the filler compressing leading to venous compression and leading to blindness. Early recognition and

taking the necessary steps to reverse the occlusion is necessary to avoid irreversible outcomes (Chen Q, 2016).

Retinal artery occlusion **:** It is a rare event that occurs after the entrance of the dermal filler (all kinds are included) into one of the distal branches of the ophthalmic artery through retrograde arterial flow. These include the angular artery and zygomatico temporal, zygomatico facial and dorsal nasal arteries in addition to supraorbital and supratrochlear arteries (Figure 4.5) .

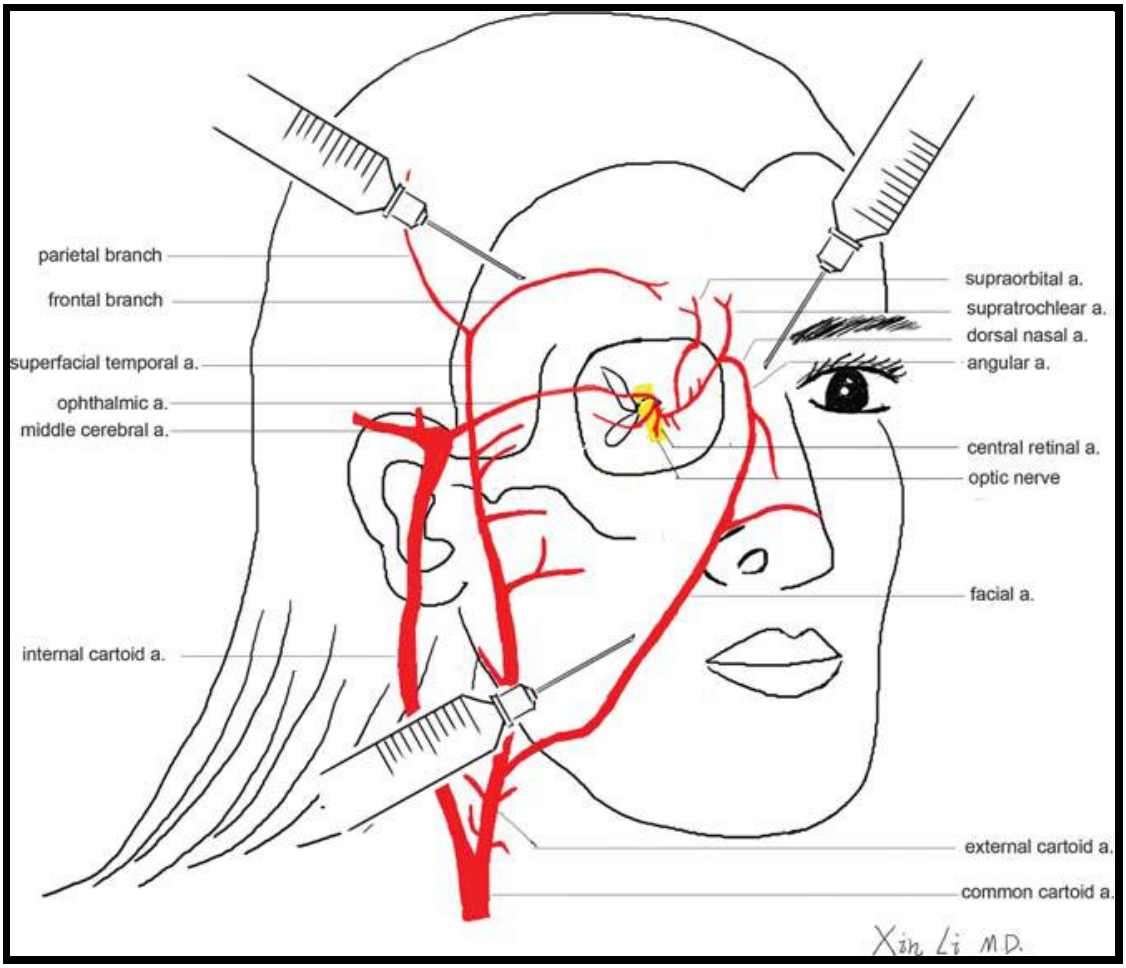

Figure 4.5. Injection risk areas that leads to retinal artery occlusion (Li X, 2015)

When one of these arteries is subject to intravascular injection exceeding intra-arterial pressure, the filler might move proximal to the origin of the central retinal artery; when the pressure is released, the material moves distally into the retinal artery, blocking blood supply to the retina and potentially causing immediate loss of vision or blurring. The facial zones that are mostly at risk are the glabellar area and forehead in addition to, nasolabial fold, nasal dorsum and temporal region. While injecting, the practitioner should be aware of the symptoms involved in ophthalmic artery occlusion to be able to take actions on time and reverse the injury. These symptoms include developed pain the involved eye, headache, nausea and sweating. If these symptoms were noticed during injection, the injector should stop at once and refer to vasodilation process by applying hot gauze with nitroglycerin paste. To avoid such an adverse event, the physician in practice should be familiar with facial vascular anatomy in the 1st place, additional precautions include aspiration before injection, using lidocaine or epinephrine or both for dilution of filler, injection slowly with lowest possible pressure and blunt cannula, avoid large volume bolus injection which should be given in periosteum plane. (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013; Ozturk CN, 2013; Li X 2015)

Tissue necrosis: Necrosis can happen after the use of any filler in general but it is more likely to occur due to particulate fillers. Mostly susceptible areas are those depending on a single arterial branch for their blood supply. Areas highly at risk include glabellar area in the 1st place and nasolabial folds. Care should also be taken when injecting near the alar groove, lips and nose. While injection process, certain visible symptoms indicate vessel embolization and can act as a warning to the practitioner to take actions. The 1st indication is the pain, but it can be a misleading sign due to the use of local anesthetics with the fillers that will block the nerve and eventually block any sensation of pain. The gold standard used as an indication is the appearance of discoloration manifested in a blanching area followed by duskiness and ecchymosis. If not treated, it will develop to reticulated erythema, purpura and ulceration and eventually scarring (Figure 4.6). The symptoms are usually featured on the spot during the injection, but in some cases, a delay can happen in showing any. At this point, any further injection should be ceased and the goal should be promoting increased blood flow to the injured area through a massage followed by compressing by warm gauze and nitroglycerin paste. Prostaglandin E1 can also be used to promote vasodilation. Medrol dose pack is given to the patient in addition to anticoagulants such as aspirin and Enoxaparin Sodium Injection. Sildenafil 100 can also come handy for vasodilation. In severe cases, physician should refer to hyperbaric oxygen.

Antibacterials and antivirals can also be used as prophylactic procedures. In case filler used was HA the hyaluronidase should be used at once. Same procedures as those of retinal artery occlusion to avoid the adverse events should be taken in addition to avoiding using local anesthetics to be able to recognize the pain and epinephrine to be able to determine the cause of blanching (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013; Souza Felix Bravo B, 2015, Chen Q, 2016).

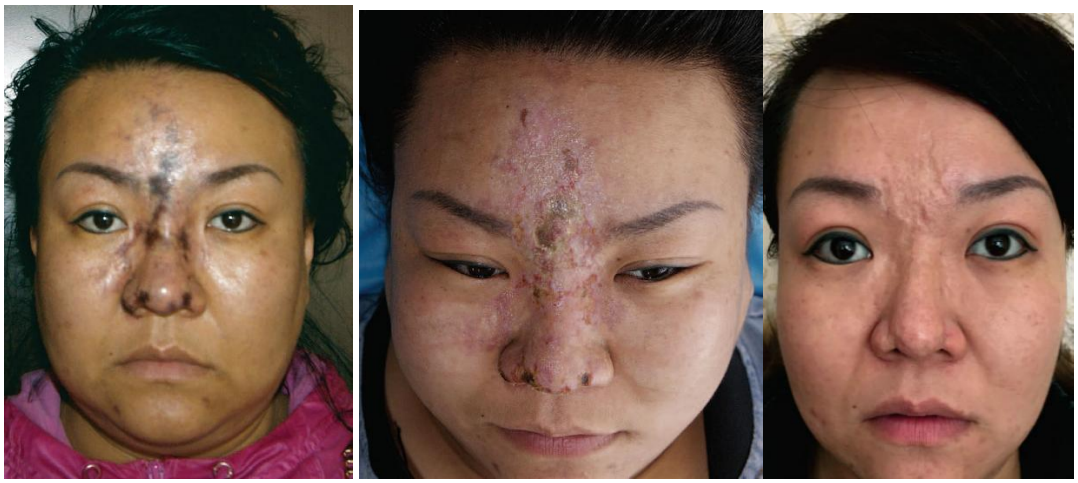

Figure 4.6. Tissue necrosis: from injection until healing (2-days, tissue repair process 9 days later, 8 months later) (Chen Q, 2016).

4.2.8 Migration

Migration of the filler is described as the presence of the filler in a distant location from the initial injected area. It is mostly due to poor injection techniques like high pressure and high volume injections. Other possible causes include gravity and muscle movement. Too superficial injection or injections in area with mobile anatomic nature like the lips (injecting CaHA into the lips) are also possible causes for filler migration. To avoid such an outcome, it is advised to perform low pressure and low volume injections in multiple treatment sessions. In case the patient suffered from such adverse event, it is advised to massage the area with the use of intra-lesional steroids or removal of the product surgically (Choi WY, 2015; Funt D, 2013; Kim JH, 2014, DeLorenzi C, 2013).

5. STANDARD GUIDELINES FOR THE USE OF DERMAL FILLERS

Treatment with dermal fillers is not a procedure that begins and ends only during the injection process. There are steps to be taken from the minute the patient decide to undergo such treatments until the follow up post treatment.

5.1 Pre-procedure considerations

Several procedures should be taken prior to any treatment which are in favor for both, the physician and the patient. It will help them make the right decision on which filler to use or whether filler treatment is suitable in the 1st place or not. Those procedures can also help avoid any adverse effects and sometimes it can be helpful in treating the complications if they occur. As a 1st step, the patient should explain the expected results and areas to be treated, and the physician should explain thoroughly the filler options for the treatment with the actual results to be expected without any exaggeration in addition to the adverse effects keeping in mind that permanent fillers come with more complicated adverse events (Bailey SH, 2011; Vedamurthy M, 2008; De Boulle, 2015; Liao J, 2013)

After that being clear, the medical history of the patient should be taken including any allergies, family medical history, medications used, and previous operations the patient might have undergone or current medical conditions that he or she might be suffering from. A medical examination should be performed emphasizing on the area of concern. At this point, the physician will be able to make the right call about the suitability of the patient as well as different fillers after considering the patient's related factors. In Table 5.1 are the conditions contraindicating or warranting caution in the use of dermal fillers (CI, contraindicated; PD, treat at physician's discretion; NAC, no apparent contraindication) (Bailey SH, 2011; Vedamurthy M, 2008; De Boulle, 2015; Liao J, 2013)

Table 5.1 Conditions contraindicating or warranting caution in the use of dermal fillers (De Boulle K, 2015)

Condition	Examples or comment	CI	PD	NAC
Active skin infection	Impetigo, herpes simplex, massive demodex folliculorum, pityrosporum, *Propionibacterium acnes*, viral warts	X		
Inflammatory conditions of the skin	Atopic patients, allergic contact dermatitis, "status cosmeticus" or sensitive skin syndrome, seborrheic dermatitis, active lichen planus, active acne rosacea		X	
Other inflammatory diseases	Pyoderma		X	
	Osteoarthritis			
Active localized infection	Ear, nose, or throat infections, dental abscess, periodontitis	X		
Active generalized infection	Gastroenteritis, urinary bladder infection	X		
Noninfectious gastrointestinal conditions	Crohn's disease, ulcerative colitis		X	
Allergy/hypersensitivity	Hypersensitivity to filler components including lidocaine, chronic urticaria, and Quincke's edema	X		
Active psoriasis arthropatic	If condition is more arthropatic: caution warranted		X	X
	If condition is more psoriatic than arthropatic: treatment is possible			
Systemic infections: viral	HIV		X	
Conditions potentially causing a Koebner response	Lichen planus, lichen nitidus, or lichen sclerosus, psoriasis, viral warts		X	
Active collagenoses	Mixed connective tissue disease	X		
	Active morphea, active systemic lupus			
Other collagenoses	Marfan syndrome, Ehlers–Danlos syndrome		X	
	Stabilized morphea			X
Immune compromise	Graft versus host disease	X		
Immune compromise	Bullous diseases		X	
Autoimmune conditions	Active Hashimoto's disease	X		
	Mixed connective tissue disease			
Autoimmune conditions	Dermatomyositis/polymyositis, lupus erythematosus, rheumatoid arthritis		X	
Transplant patients Immunosuppressive therapy	Heart, kidney, liver, bone marrow transplant: beware of increased risk of infections		X	
Thyroid dysfunction	Not a contraindication to treatment, but physician needs to be aware that eyelid swelling is common (unrelated and unprovoked by filler use)		X	
Metabolic disorders	Diabetes, porphyria			X
Catabolic status		X		
Cachexic state	Does not contraindicate treatment, but product may be more visible in patients who lack subcutaneous fat and have thin tissue coverage		X	
Conditions affecting skin pigmentation	Melasma and post-inflammatory hyperpigmentation		X	
Skin pigmentation/depigmentation	Fitzpatrick Types 5 and 6 skin, vitiligo, and albinism			X
Systemic infections: bacterial	Tuberculosis	X		
Active anticoagulant medication	Thrombolytics	X		
Hemostatic or coagulation disorders	Hemophilia, hemoglobin pathology, thalassemia	X		
Cutaneous collagenoses	Chronic discoid lupus erythematosus, active but not end-stage scleroderma		X	
Food intolerance			X	
Bariatric gastric sleeve surgery	Potentially reduced time of esthetic effect			X

If needed, prophylactic agents should be given like antivirals in case of Herpes Simplex Virus (HSV). In other cases, the patient might need to stop some medications he or she is on, if possible, like anticoagulant agent 1 week in advance to minimize bruising. If the patient is planning to undergo any other procedures, the timing should be taken into consideration. In case of any intention to undergo botulinum toxin treatment, it is preferred to take place 2 weeks before dermal filler treatment. In case of laser or IPL, they should be planned 1-2 weeks pre or post injection. It is advised to take preoperative picture for the assessment of treatment effects and any subsequent complication, and sometimes, for medicolegal purposes. Finally, patient should sign an informed consent (Bailey SH, 2011; Vedamurthy M, 2008; De Boulle, 2015; Liao J, 2013)

5.2. Intraoperative procedures

Before anything, the absolute and thorough knowledge of the injector of the facial anatomy and areas in risk, especially the distribution of the facial arteries and nerves, is out of question. The fact the minor changes variations between individuals can be present, sometimes due to dental or facial surgery. Aseptics should never be ignored. The area to be treated along with the surrounding skin should be cleaned with topical antiseptics like chlorhexidine or iodine. The injector should take care of his own hygiene as well by washing the hands, removing any accessories in the hand and wearing gloves. Aspiration should be performed before injection as a prophylactic measure, especially in highly vascularized areas. The injector should be able to make the right decision about using anesthesia and the injection technique based on each case conditions (Bailey SH, 2011; Vedamurthy M, 2008; De Boulle, 2015; Liao J, 2013).

5.3. Post-procedural precautions

Even if everything looked safe and satisfying once the dermal filler treatment ends, some further steps to be taken (for at least 24 hours post treatment) can ensure more safety and might help to avoid certain adverse events. Extreme temperatures should be avoided, the patient should stay away from extreme hot or cold. Touching or massaging the treated area or even applying makeup and cosmetics should be avoided as well. Patient should not be doing any intense exercise or effort. It is best if patient could preserve an elevated posture as much as possible. Finally, patient is expected to go back to the clinic for follow up in 2-4 weeks (Bailey SH, 2011; Vedamurthy M, 2008; De Boulle, 2015; Liao J, 2013).

6. MEDICAL ERRORS AND MALPRACTICES ACCORDING TO LEBANESE LAW

The Lebanese medical law differentiates between a yielded complication and a medical error. Medical errors are errors committed, as a result of inexperience or incompetence, by the practicing physician or the assisting staff. Medical errors could also be the result of an experimental and new professional practice or treatment method, an emergency requiring fast treatment at the expense of precision, or caused by the complex nature of the treatment. Accordingly, the physician must always respect and abide by general and professional ethics. In this regard, national legislations in force stipulate the obligation to abide by professional ethics and maintain confidentiality. These legislations were issued in 1994 and carry the number 288 in addition to Lebanese medical law issued in 1979.

Physicians are allowed to practice medicine through the Order of Physicians. In this regard, the law aiming to establish two orders for physicians in Lebanon states that a Professional Investigations Committee should be formed to handle the examination of the issues and litigations arising between physicians, or between physicians and their patients, and referred to this committee by the Order president or council. Cases of medical errors are part of the cases referred to this committee. This committee shall conduct the required investigations when necessary, and report to the Order council. When needed, it may draw on the expertise of physicians, university professors and the Order's legal advisor. Cases of misconduct are referred to the disciplinary board in the following cases:

- Upon a complaint filed by the Ministry of Public Health or by victims of medical or non medical errors
- Upon a request of the president
- Upon the request of physicians considering themselves subject to unfair accusations. These physicians place their cases to be examined by the disciplinary board.

When physicians are subject to legal prosecution, the Order shall provide a medical opinion within fifteen days, determining whether the alleged offense is a result of practice of the profession. In this case, the prosecuted physicians are subject to questioning before the Order president or his/her representative for this case. Pursuant to this article, prosecuted physicians may not be placed under remand for an offense resulting from professional practice prior to the provision of the medical opinion of the Order within the period above mentioned. This law assigned the task of conducting the necessary investigations to a committee formed of members

of the Order council. The disciplinary board shall have the authority to take the appropriate measures against the prosecuted physician. These measures are as follows:

- Warning.
- Admonition.
- Temporary suspension from practice for no longer than six months.
- Permanent ban from the practice of medicine.

To convict a physician, the committed error must be the result of neglect, lack of attention or caution, must be unintentional and serious, in other words, such error would not have been committed under similar circumstances, by a physician who knows his duties well. The error committed by the physician must be a ‘faute caractérisée’ and the judge may not hold the physician responsible unless a ‘faute caractérisée’ is identified resulting from the lack of knowledge by the physician (Lebanon Order of Physicians, 2017).

7. MATERIALS AND METHODS

This study was conducted in Lebanon in which it was based on 2 major procedures:

- Data collection
- Survey

7.1. Materials

Data for previously recorded complications of dermal fillers was collected from 5 clinics in Saida and Beirut-Lebanon during the period of February 9 to April 10, 2017. In addition, a survey was conducted, including 5 demographic questions and 11 about awareness and knowledge, to investigate the awareness of the public about the different types of dermal fillers and their complications at the same period.

7.2. Methods

For data collection related to previous records indicating dermal filler complications, we aimed to visit 5 clinics distributed in Saida and Beirut. With the permission of the physician in charge, we checked the cases they had for patients who have suffered from certain adverse events due to dermal fillers during the last 10 years, and discussed each case separately. Our field of interest was the age of the patient, kind of dermal filler used, the yielded complication and the treatment.

As for the conducted survey, it was done in a face to face approach starting with a signed informed consent from all participants informing them about the survey and its purpose. Our public was females from different age groups and backgrounds where questionnaires, including a demographic section and awareness section, were distributed to each of them.

Types of dermal fillers obtained from patients' records, along with demographic characteristics and knowledge about the filler applications of surveyed subjects will be classified and analyzed using appropriate statistical test method.

Prior to the study, we took the approval of the Near East University Scientific Research Advisory and Ethical Committee (Dated 18.01.2017; 2017/43, Project Nr. 360).

8. RESULTS AND DISCUSSION

8.1 Collected Dermal Fillers Related Complications Cases

A total of 18 serious cases, in addition to cases with slight self-resolvable adverse events, were collected from 5 different clinics in Saida and Beirut with the permission of the physician in charge. Few of the cases were complications due to dermal filler treatment at the clinic itself, whereas most of the cases referred to these clinics after suffering from adverse event due to dermal fillers injected by other physicians whose patients have lost trust in.

The identity of each patient was discrete but I was able to check other information including age, area of treatment, filler used and yielded complications. All the physicians agreed that most of the serious complications are always due to permanent fillers rather than the biodegradable ones, this is why most of them were insisting on using hyaluronic acid solely due to favorable risk margin, satisfying result, more affordable than other biodegradable fillers like calcium hydroxylapatite and the problem can always be resolved using hyaluronidase. However, they all agreed that complications are due to technique rather than the product itself.

Females from all age groups chose to undergo dermal filler procedures, in which the age range of females with collected complications (n=18) varied from 22 years old up to 55 years old with an average of 40 years old. The fillers used were either hyaluronic acid or PMMA. The cases varied from simple adverse events such as erythema to more severe complications and serious events as serious as skin necrosis. During the collection of dermal fillers complications from the selected clinics in Saida and Beirut, the physicians agreed that, during their practice, approximately 1-2% of patients underwent filler treatment, suffered from complications. Table 8.1 lists all the collected cases along with the fillers used and treatment approaches. In addition to these cases, there was a common note from all the visited clinics stating that injection of HA in different areas to different females with different age groups almost always resulted in stiffness and redness that resolved by itself.

Table 8.1 Collected cases from the clinics in Saida and Beirut-LEBANON.

Type of filler	Area of injection	Type of Complication	Treatment approach
HA	Nasolabial folds	Severe infection	Hyaluronidase+ IV antibiotics
HA	Nasolabial folds	Allergic reactions	IV corticosteroids
PMMA	Lips	Scar tissue	Surgical excision
HA	Forehead	Granuloma	Hyaluronidase
PMMA	Cheeks	Skin necrosis	Vasodilating agents +antibiotics but the patient did not fully recover
PMMA	Cheeks and nasolabial folds	Infection, abscess formation and moving granuloma	1st drainage leading to a scar, then surgical excision, not totally cured
HA	Lips	Nodule above the lip	Resolved by itself within a year
HA	Nasolabial folds	Telangiectasia	Treatment attempts with laser, not totally cured
HA	Lips	Herpetic outbreak in spite of the prophylactic procedures taken in advance	Antiviral agents
HA	Lips	Herpetic outbreak	Antiviral agents
HA	Nasolabial folds	Migration of nodule to forehead	Surgical excision
HA	Glabellar area	Skin necrosis	vasodilation agents+antibiotics in addition to anticoagulants
PMMA	Lips	Granuloma	Surgical excision
HA	Lips	Herpetic outbreak	Antiviral agents
PMMA	Back of the hand	Foreign body granulomas	Surgical excision
PMMA	Under eye area	Granuloma	The patient did not accept and surgical intervention
PMMA	Lips	Multi nodules 6 years later	Surgical excision but did not fully recover
PMMA	Cheeks	Scar tissue	The patient is still trying to find a nonsurgical solution

According to our cases collected, 10 out of 18 cases were due to hyaluronic acid but this is due to its wide use since it is much more preferred than PMMA by the physicians. On a statistical level, percentage of complications due to HA fillers is much less than those of PMMA. In spite of the low percentage of complications, it is still an undeniable fact that adverse effects are not uncommon following dermal filler injections, even after a long period.

In a previous review of long-term adverse effects associated with the use of chemically-modified animal and non-animal source hyaluronic acid dermal fillers, the complications collected matched our results from different aspects. From the collected cases, most vulnerable area was the lips with similar adverse events to our collected cases including herpetic outbreaks. It showed that severe and delayed complications with HA are less common. It showed the results a review of Restylane complications reported to the manufacturer in 1999 and 2000, documenting 1 adverse reaction in every 650 to 1800 patients in which most of them are considered to be very mild, self resorbable events. There were two cases of injection site necrosis in the glabellar area, as well as "rare reports of localized granulomatous reactions, bacterial infections, acneiform and cystic lesions". This percentage highly matches the reports from the visited clinics In Lebanon. The result of this review similarly states that complications for HA is always a possibility in spite of its low overall incidence of long term side effects. (Edwards PC, 2007)

Another review done in the University of Ferrara, Italy, about the complications following permanent fillers use lead to a conclusion that these complications are mostly granulomatous reactions with a delayed onset possibility, which is also shown in our collected cases, and suggesting the use of biodegradable substances for injection as a safer alternative, as advised by the physicians visited in Lebanon. (Zollino I, 2014)

8.2. Awareness of Lebanese Females Related to Different Aspects of Dermal Fillers

The survey included 300 females from different age groups and backgrounds. They answered some demographic questions and others about their preference to undergo filler procedures, their acquaintance with their types and their awareness of the possible risks. Table 8.2 includes the demographic characteristics of the participants.

Table 8.2 Main demographic characteristics of participants

Age			Educational level			Income ($)		
Age groups	**N**	**%**	**Level**	**N**	**%**	**Groups**	**N**	**%**
≤ 24	73	24.3	≤ high school or equivalent	55	18.3	< 500	61	20.3
25-34	98	32.7	Bachelor or equivalent	196	65.3	500-1000	71	23.7
35-44	58	19.3	Master or equivalent	41	13.7	1001-2000	114	38.0
45-54	39	13.0	PhD or equivalent	8	2.7	2001-3000	37	12.3
≥ 55	32	10.7				> 3000	17	5.7

According to our survey results, 88% of the participants were aware of the dermal fillers in general, in which 31.7% had actually undergone dermal filler procedures while 63% considered the possibility of undergoing such treatments in the future. Many factors affected those results including age, educational level and income (Tables 8.3-8.6). The percentage of people underwent dermal fillers treatment varied with the different age groups in ascending manner, the bigger the age group, the higher the percentage was; the same results apply to different income groups in the same manner, unlike different educational levels where no significance is seen among the different groups. The difference in age groups effect is also seen in the variation of area treated; for example young females, below 24, were interested in having fuller lips only, then they tend to fill their nasolabial folds in their early thirties in addition to the cheeks, with progressing age, other areas are included like forehead, under eye area and back of the hands. We cannot say the same thing about the future considerations for participants from different groups, where their differences did not affect their desire or non-desire for future plans in having dermal fillers.

An interesting result in this survey was the percentage of participants who chose fillers treatment and were aware of the material used where only 48.4% were aware of the type of injected filler. This result varies with different educational levels as seen in Table 8.3 where the asymptotic significance is <0.05 which indicates the existence of significance among the different groups.

Table 8.3-A . Educational level vs Awareness of dermal filler type

Edu. Level		Aware of Type		Total
		Yes	No	
≤ high school or equivalent	N	5	50	55
	% within educational level	9.1%	90.9%	100%
	% within aware of type	10.6 %	19.8%	18.3%
	% of total count	1.7%	16.7%	18.3%
Bachelor or equivalent	N	29	167	196
	% within educational level	14.8%	85.2%	100%
	% within aware of type	61.7%	66.0%	65.3%
	% of total count	9.7%	55.7%	65.3%
Master or equivalent	N	8	33	42
	% within educational level	19.5%	80.5%	100%
	% within aware of type	17.0%	13.0%	13.7%
	% of total count	2.7%	11.0%	13.7%
PhD or equivalent	N	5	3	8
	% within educational level	62.5%	37.5%	100%
	% within aware of type	10.6%	1.2%	2.7%
	% of total count	1.7%	1.0%	2.7%
Total	N	47	253	300
	% within educational level	15.7%	84.3%	100%
	% within aware of type	100%	100%	100%
	% of total	15.7%	84.3%	100%

Table 8.3-B. Chi-Squares Tests

	Value	df	Asymp. Sig. (2 sided)
Pearson Chi-Square	15.652a	3	.001*
Likelihood Ratio	11.5853457398667	3	.009
Linear-by-Linear Association	9.48646468049642	1	.002
N of Valid Cases	300		

* Shows statistical significance since its value is ≤ 0.05

The survey showed an almost equal percentage about the public's belief in the safety of the dermal fillers with 51.3% believing that they are safe to be used. This percentage is highly affected by educational level with more belief in their safety as the level of education gets higher as shown in Table 8.4-A and Table 8.4-B (p. Upon asking about the risks of dermal fillers, 55.3% of the answers were not sure or not familiar with them, 28.7 % believed that they are totally safe with no risks what so ever, and the rest gave different answers like allergy, infection or even unnecessary distorted over filling.

Table 8.4-A Educational level vs safety belief

Educational Level		**Safety belief**		**Total**
		Yes	No	
≤ high school or equivalent	N	15	40	55
	% within educational level	27.3%	72.7%	100%
	% within safety	9.7%	27.4%	18.3%
	% of total count	5.0%	13.3%	18.3%
Bachelor or equivalent	N	107	89	196
	% within educational level	54.6%	45.4%	100%
	% within safety	69.5%	61.0%	65.3%
	% of total count	35.7%	29.7%	65.3%
Master or equivalent	N	26	15	41
	% within educational level	63.4%	36.6%	100%
	% within safety	16.9%	10.3%	13.7%
	% of total count	8.7%	5.0%	13.7%
PhD or equivalent	N	6	2	8
	% within educational level	75.0%	25.0%	100%
	% within safety	3.9%	1.4%	2.7%
	% of total count	2.0%	0.7%	2.7%
Total	N	154	146	300
	% within educational level	51.3%	48.7%	100%
	% within safety	100%	100%	100%
	% of total	51.3%	48.7%	100%

Table 8.4-B Chi-Squares Tests for the correlation between the education level and safety belief

	Value	df	Asymp. Sig. (2 sided)
Pearson Chi-Square	17.767a	3	.000*
Likelihood Ratio	18.3141138934333	3	.000
Linear-by-Linear Association	15.0503301218944	1	.000
N of Valid Cases	300		

* Shows statistical significance since its value is ≤ 0.05

Participants from different ages seemed to agree about the personal motives and general public motives that might push them to consider dermal filling. Most of them agreed that it is all about self improvement and more youthful looks, while only around 15% believe in the effect of the media in this field; these results are illustrated in details in Table 8.5 and 8.6.

Table 8.5 Personal motives for each participant

Motives	Frequency	Percentage
Self-improvement	103	34.3%
Confidence boost	61	20.3%
Corrective	136	45.3%
Total	300	100%

Table 8.6 General motives among the public

Motives	Frequency	Percentage
Boost self esteem	58	19.3 %
More youthful look	185	61.7 %
Media	46	15.3 %
Peer pressure	11	3.7 %
Total	300	100 %

Based on the results of the conducted survey, dermal fillers are so popular among females in Lebanon regardless of their age or background. Although maintaining a youthful look is the main reason behind such procedures, seeking perfection is a main issue also which clearly shows in the results of using dermal fillers even at very young ages. The participants did not believe much in the effect of the media in their decisions, meanwhile many females below 30 used dermal fillers to improve some of their facial features such as fuller lips, which, according to my point of view, is a result of the perfect image imposed by the media.

Comparing these results with those of ASAPS 2016 Cosmetic Surgery National Data Bank Statistics, we can see that they match to a big extent concerning the percentage of people undergoing dermal filler procedures at different age groups as shown in Fig. 8.1 and Table 8.7-A and 8.7-B. This is just another proof that the results of age distribution for dermal filler procedures in Lebanon are not unique which indicates the effect of the international media.

Table 8.7-A Age Distribution for Dermal Filler Procedures in Lebanon

Age Group		Undergone any procedure		Total
		Yes	No	
≤ 24	N	4	69	73
	% within Age Group	5.5%	94.5%	100%
	% within undergone any procedure	4.2%	33.7%	24.3%
	% of total count	1.3%	23.0%	24.3%
25-34	N	36	62	98
	% within Age Group	36.7%	63.3%	100%
	% within undergone any procedure	37.9%	30.2%	32.7%
	% of total count	12.0%	20.7%	32.7%
35-44	N	27	31	58
	% within Age Group	46.6%	53.4%	100%
	% within undergone any procedure	28.4%	15.1%	19.3%
	% of total count	9.0%	10.3%	19.3%
45-54	N	18	21	39
	% within Age Group	46.2%	53.8%	100%
	% within undergone any procedure	18.9%	10.2%	13.0%
	% of total count	6.0%	7.0%	13.0%
≥ 55	N	10	22	32
	% within Age Group	31.3%	68.6%	100%
	% within undergone any procedure	10.5%	10.7%	10.7%
	% of total count	3.3%	7.3%	10.7%
Total	N	95	205	300
	% within Age Group	31.7%	68.3%	100%
	% within undergone any procedure	100%	100%	100%
	% of total	31.7	68.3%	100%

Table 8.7-B Chi-Squares Tests

	Value	df	Asymp. Sig. (2 sided)
Pearson Chi-Square	34.022a	4	.000*
Likelihood Ratio	41.0001570715113	4	.000
Linear-by-Linear Association	14.0207538390777	1	.000
N of Valid Cases	300		

* Shows statistical significance since its value is ≤ 0.05

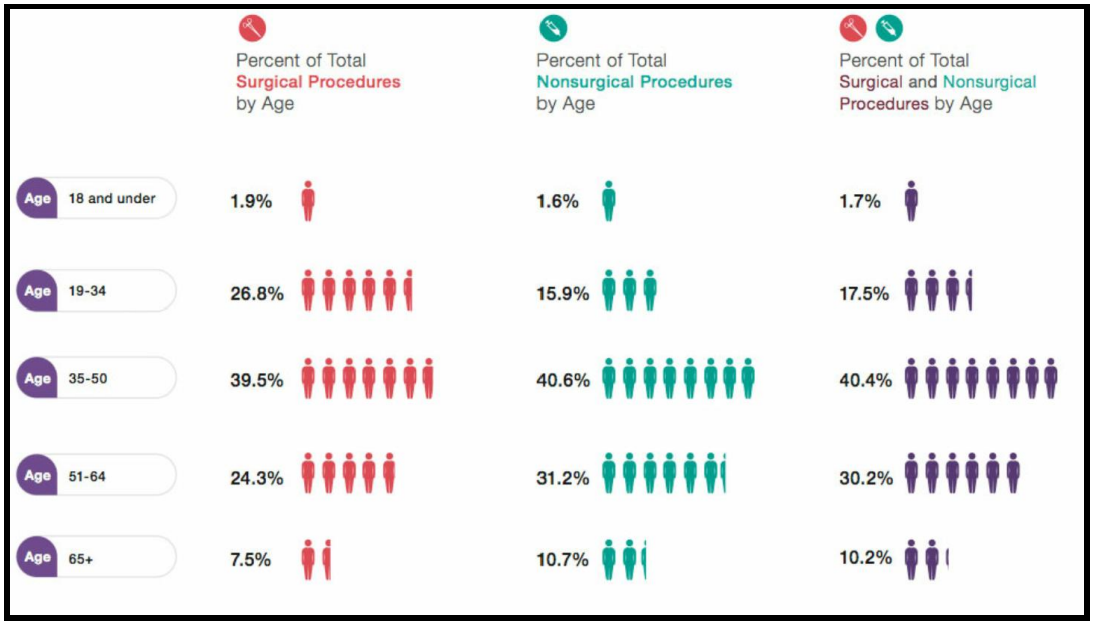

Fig. 8.1 ASAPS 2016 Age Distribution for Cosmetic Procedures

Another survey conducted and cosponsored by the American Society for Dermatologic Surgery and Dermik Laboratories, a business of Sanofi-Aventis U.S. LLC contained 383 female participants aged 35 to 69. Among the 383 participants, 16.7 % undergone dermal filler procedures vs 31.7% in our conducted survey with a lower age mean. This is an indication that Lebanese females in general have a bigger interest in the image perfection for women. Another result is percentage the women interested in having such procedures in the future with 78.3% vs 63.7% in our survey. This result considered to be very close to our

survey as the distribution among the different educational levels is almost the same in the 2 surveys as shown in Table 8.8. (Weinkle S, 2010)

Table 8.8. Distribution of educational levels among future considerations and filler users in Lebanon survey and the American Society for Dermatologic Surgery and Dermik Laboratories Survey

Educational level	Future considerations		Filler users	
	Lebanon	USA	Lebanon	USA
High School	11%	9%	11.6%	11%
Bachelor	68.6%	74%	67.4%	64%
Postgraduate	20.4%	17%	21.1%	25%

The survey shows a great lack of awareness concerning this issue even in higher educational levels. It can be seen in the amount of participants who did not show any interest in being informed about the injected material prior to usage. Another evidence is the misconception about risks of dermal fillers where they were either considered to be totally safe or having no idea about the possible adverse events.

9. CONCLUSION

Dermal filler, to a big extent, are considered to be safe with a small margin of possibility to cause adverse events, especially when biodegradable products are used. The majority of these adverse events are due to poor technique and injector inexperience rather than the product itself. People might be with or against such procedures, but the fact that the use of the fillers is dramatically increasing as a means for pursuit of fountain of youth cannot be ignored. As a result, public should be more informed to gain more awareness regarding this field through studies and articles rather than letting them to be mislead by the improper sources.

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11. APPENDIX

NEAR EAST UNIVERSITY

INSTITUTE OF HEALTH SCIENCES-DEPARTMENT OF TOXICOLOGY, NICOSIA-TRNC

"Dermal Fillers: Risks, Awareness and Reported Complications"

SURVEY FORM

Participant no._____ Date ___/___/_____

Dear Participant;

This study is conducted by Near East University, Toxicology department, to acquire more knowledge about the safety and risks of dermal fillers, and to investigate the awareness of the public regarding this issue. All the answers collected will be used for the benefit of this study. The identity of all participants will be completely confidential.

Principal Investigator: Prof. Dr. Şahan SAYGI, E-mail: sahan.saygi@neu.edu.tr

Assistant Investigator: Res. Assist. Noura SABEHAAYOUN

I read the previous conditions and I agree to participate in this survey ☐

I. DEMOGRAPHIC DATA

1. What is your age? …….. years old

2. What is your educational level?

	≤ High school degree or equivalent
	Bachelor or equivalent
	Master or equivalent
	Doctoral or equivalent

3. Which of the following best describes your current occupation?

	Student
	Teacher / Academician
	House wife
	Private Business Owner
	Worker
	Retired
	Other (Please specify:……)

4. Do you have any educational back ground in health care sciences (physician, pharmacy, dentistry, nursing, lab technician or else) ? Please specify.

……

5. What is your approximate average household income/month?

	≤ 500 $
	500 - 1000 $
	1000 - 2000$
	2000 - 3000$
	≥ 3000$

II. KNOWLEDGE AND AWARENESS

6. Have you ever heard about dermal fillers?

   - Yes
   - No

7. Have you ever undergone any dermal filler procedure?

   - Yes
   - No

8. If yes, were you aware of type of dermal filler used?

   - Yes (please specify)
     …….
   - No

9. In which part of your body you used the filler?

	Lips
	Nasolabial area
	Cheeks
	Under eye area
	Forehead
	Back of the hands
	Others (please specify……)

10. If No, would you consider having any in the future?

- Yes
- No

11. What would be the biggest reason for having dermal fillers?

	Self Improvement
	Confidence boost
	Corrective
	Others

12. What do you think is the main reason that makes people go for dermal filling?

	Boost self-esteem
	More youthful look
	Media
	Peer Pressure
	Others

13. Do you believe that dermal fillers are safe to use?

- Yes
- No

14. If yes, what do you think are the risks of dermal filling if there is any?

…….

15. Have you or anyone you know suffered from any kind of complications due to dermal fillers?

    - No
    - Yes

16. If yes kindly mention the type of the filler, site of injection and complication.

    ……
    ……

    ……
    ……

17. How do you evaluate this survey

    - Good
    - Fair
    - Poor

THANK YOU FOR YOUR COOPERATION

T.R.N.C.

NEAR EAST UNIVERSITY

HEALTH SCIENCES INSTITUTE

DERMAL FILLERS: RISKS, AWARENESS AND REPORTED COMPLICATIONS

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Nicosia, T.R.N.C. 2017