

## Bölüm 6

### FERTİLİTE KORUYUCU YAKLAŞIMLAR

Volkan EMİRDAR<sup>1</sup>

Günümüzde yılda 100.000 den fazla yeni kanser vakası bildirilmekle birlikte, 40 yaş altı reproduktif dönem hastalar bu vakaların %3 ünü oluşturmaktadır(Cronin & ark., 2018). Reprodüktif dönemde meme kanseri kadın kanserlerinde birinci sırayı almaktadır. Kanser tedavilerindeki yenilikler ile kür ve sağkalım oranları artmış, tedavi sonrası gonadotoksik tedavilerin yol açabileceği fertilitate kaybı riskine karşı üremenin korunması alanında yeni yaklaşımlar hız kazanmıştır. Bu modalitelerin yaygınlaşması için sağlık profesyonellerinin doğru zamanda, doğru bilgilendirme ve yönlendirmeler ile hastaları gonadotoksik tedaviler öncesinde fertilitate koruyucu tedaviler için uygun birimlere yönlendirmesi önem kazanmıştır. Fertilitate koruyucu yaklaşımların artık gonadotoksik tedavi alacak tüm hastalar ile detaylı şekilde tartışılması ve hastaların tedavi öncesi fertilitate koruyucu yaklaşımlar için üreme sağlığı uzmanına yönlendirilmesi konusunda 2006 yılında Amerikan Üreme Endokrinolojisi Derneği (ASRM) görüş bildirmiştir (Lee & ark., 2006). Yeni yaklaşımlar ile fertilitate korunması konusunda çok büyük bir yol kastedilmesine rağmen farkındalık maalesef hala istenilen seviyeye ulaştırılamamıştır. Farkındalığın arttırılabilmesi için bu hasta grubu ile çalışan tüm sağlık profesyonellerinin multidisipliner işbirliği içerisinde hastaları belirli algoritmalar ile üreme sağlığı uzmanı ile buluşturmaları en önemli basamağı oluşturmaktadır (Quinn & ark., 2008; Quinn & ark., 2009a, 2009b).

Etkili bir fertilitate koruyucu program için medikal onkolog, radyasyon onkoloğu, cerrahi onkolog, reproduktif endokrinolog ve ürolog arasında sağlıklı bir iletişim olması gereklidir. Bu hasta grubu ile primer çalışan onkologlar; tedavi sonrası oluşabilecek fertilitate kaybı risklerini hastalar ile konuşup, hastaları ayrıntılı bilgilendirmeli ve tedavi öncesi uygulanabilecek yaklaşımlar için reproduktif endokrinolog ve ürologlara hastaları doğru zamanda yönlendirme hususunda başlıca rol alırlar. En ideal yaklaşım adolesan ve reproduktif dönemdeki tüm kanser hastalarının gonadotoksik tedaviler öncesinde fertilitate prezervasyonu konusunda uzman üreme sağlığı uzmanı ve ürologlara vakit kaybetmeden yönlendirilmesi, hastanın hastalığının seyri ve prognozu gözönünde bulundurularak ilgili tüm branşların multidisipliner işbirliği ile hasta için en uygun yaklaşımın birlikte se-

<sup>1</sup> Kadın Hastalıkları ve Doğum Uzmanı, İzmir Medicalpark Hastanesi, Kadın Hastalıkları ve Doğum Departmanı, e-mail: volkanemirdar@yahoo.com

## ERKEK HASTALAR

### Testis Dokusu ve Sperm Kriyoprezervasyonu

Erkek hastalarda sperm kriyoprezervasyonu temel fertilitate prezervasyon tekniğini oluşturmaktadır. Postpubertal erkek hastalarda kanser tedavisi öncesi semen uygun yöntemlerle alınarak kriyoprezervasyon işlemleri uygulanmalıdır (D. Ohl & ark., 2001). Semende yeterli ve sağlıklı sperm elde edilemediği durumlarda invaziv yöntemler testis dokusundan sperm elde edilerek kriyoprezervasyon işlemi uygulanabilir (D. Ohl & ark., 2008).

Testis kanseri nedeniyle cerrahi planlanan hastalar yine tedavi öncesi bilgilendirilmeli ve sperm kriyoprezervasyonu önerilmelidir. Yine konjenital olarak veya geçirilmiş enfeksiyonlara bağlı testis boyutlarında küçüklük veya sperm sayısı ve hareket azlığı, sperm şekil bozukluğu gibi durumlarda ileride karşılaşılabilecek muhtemel azospermi riskine karşı sperm kriyoprezervasyonu fertilitate koruyucu yöntem olarak hastalara önerilmelidir.

Yine karşılaşılan obstruktif ve non-obstruktif azospermi olgularında testis dokusu dondurma yöntemi geçerliliği kanıtlanmış bir fertilitate koruyucu yöntem olarak günümüzde uygulanmaktadır (Meirow & Schenker, 1995). Prepubertal erkek çocuklardan kriyoprezervasyon için sperm örneği alınamadığından deneysel de olsa testis dokusu kriyoprezervasyonu tek fertilitate koruyucu seçenek olarak uygulanmaktadır. İlerleyen yıllarda yeni teknolojiler ile çözülen testis dokusundan elde edilecek olan spermatojenik kök hücreden sperm üretilmesi ile ilgili çalışmalar devam etmekte olup henüz başarılı sonuçlar bildirilmemiştir.

## KAYNAKLAR

1. Bedaiwy, Mohamed A., Ahmed M. Abou-Setta, Nina Desai, William Hurd, David Starks, Sherif A. El-Nashar, Hesham G. Al-Inany, and Tommaso Falcone. 2011. "Gonadotropin-Releasing Hormone Analog Cotreatment for Preservation of Ovarian Function during Gonadotoxic Chemotherapy: A Systematic Review and Meta-Analysis." *Fertility and Sterility* 95 (3): 906–914.e4. <https://doi.org/10.1016/J.FERTNSTERT.2010.11.017>.
2. Bedoschi, Giuliano M., Felipe Oliveira de Albuquerque, Rui Alberto Ferriani, and Paula Andrea Navarro. 2010. "Ovarian Stimulation during the Luteal Phase for Fertility Preservation of Cancer Patients: Case Reports and Review of the Literature." *Journal of Assisted Reproduction and Genetics* 27 (8): 491–94. <https://doi.org/10.1007/s10815-010-9429-0>.
3. Borini, A, PEL Setti, P Anserini, R De Luca, L De Santis - Fertility and sterility, and undefined 2010. n.d. "Multicenter Observational Study on Slow-Cooling Oocyte Cryopreservation: Clinical Outcome." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028209039491>.
4. Cobo, A, M Kuwayama, S Pérez, A Ruiz, A Pellicer - Fertility and sterility, and undefined 2008. n.d. "Comparison of Concomitant Outcome Achieved with Fresh and Cryopreserved Donor Oocytes Vitriified by the Cryotop Method." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028207012186>.

5. Cobo, A, M Meseguer, J Remohí - Human reproduction, and undefined 2010. n.d. "Use of Cryo-Banked Oocytes in an Ovum Donation Programme: A Prospective, Randomized, Controlled, Clinical Trial." *Academic.Oup.Com*. Accessed January 27, 2019. <https://academic.oup.com/humrep/article-abstract/25/9/2239/2915517>.
6. Cobo, Ana, Javier Domingo, Sonia Pérez, Juana Crespo, José Remohí, and Antonio Pellicer. 2008. "Vitrification: An Effective New Approach to Oocyte Banking and Preserving Fertility in Cancer Patients." *Clinical and Translational Oncology* 10 (5): 268–73. <https://doi.org/10.1007/s12094-008-0196-7>.
7. Cronin, Kathleen A., Andrew J. Lake, Susan Scott, Recinda L. Sherman, Anne Michelle Noone, Nadia Howlader, S. Jane Henley, et al. 2018. "Annual Report to the Nation on the Status of Cancer, Part I: National Cancer Statistics." *Cancer* 124 (13): 2785–2800. <https://doi.org/10.1002/cncr.31551>.
8. Dolmans, MM, C Marinescu, P Saussoy - Blood, and undefined 2010. n.d. "Reimplantation of Cryopreserved Ovarian Tissue from Patients with Acute Lymphoblastic Leukemia Is Potentially Unsafe." *Am Soc Hematology*. Accessed January 27, 2019. <http://www.bloodjournal.org/content/early/2010/07/01/blood-2010-01-265751.short>.
9. Donnez, J, MM Dolmans, D Demylle, P Jadoul, C Pirard - The Lancet, and undefined 2004. n.d. "Livebirth after Orthotopic Transplantation of Cryopreserved Ovarian Tissue." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S014067360417222X>.
10. Donnez, J, P Jadoul, ... J Squifflet - Best practice & research, and undefined 2010. n.d. "Ovarian Tissue Cryopreservation and Transplantation in Cancer Patients." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S1521693409001175>.
11. Donnez, J, J Squifflet, P Jadoul, D Demylle - Fertility and sterility, and undefined 2011. n.d. "Pregnancy and Live Birth after Autotransplantation of Frozen-Thawed Ovarian Tissue in a Patient with Metastatic Disease Undergoing Chemotherapy and Hematopoietic." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028210028438>.
12. Donnez, Jacques, Sherman Silber, Claus Yding Andersen, Isabelle Demeestere, Pascal Piver, Dror Meirou, Antonio Pellicer, and Marie-Madeleine Dolmans. 2011. "Children Born after Autotransplantation of Cryopreserved Ovarian Tissue. A Review of 13 Live Births." *Annals of Medicine* 43 (6): 437–50. <https://doi.org/10.3109/07853890.2010.546807>.
13. Ethics, The, and Reproductive Medicine. 2013. "Fertility Preservation and Reproduction in Patients Facing Gonadotoxic Therapies : A Committee Opinion." *Fertility and Sterility* 100 (5): 1224–31. <https://doi.org/10.1016/j.fertnstert.2013.08.041>.
14. Fadini, R, MB Dal Canto, ... MM Renzini - Reproductive, and undefined 2009. n.d. "Effect of Different Gonadotrophin Priming on IVM of Oocytes from Women with Normal Ovaries: A Prospective Randomized Study." *Rbmojournal.Com*. Accessed January 27, 2019. [https://www.rbmojournal.com/article/S1472-6483\(10\)60168-X/abstract](https://www.rbmojournal.com/article/S1472-6483(10)60168-X/abstract).
15. Friedler, S, O Koc, Y Gidoni, A Razieli, R Ron-El - Fertility and sterility, and undefined 2012. n.d. "Ovarian Response to Stimulation for Fertility Preservation in Women with Malignant Disease: A Systematic Review and Meta-Analysis." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S001502821102680X>.
16. Gracia, CR, MD Sammel, E Freeman, M Prewitt - Fertility and sterility, and undefined 2012. n.d. "Impact of Cancer Therapies on Ovarian Reserve." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028211027257>.

17. Green, Daniel M., John A. Whitton, Marilyn Stovall, Ann C. Mertens, Sarah S. Donaldson, Frederick B. Ruymann, Thomas W. Pendergrass, and Leslie L. Robison. 2002. "Pregnancy Outcome of Female Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study." *American Journal of Obstetrics and Gynecology* 187 (4): 1070–80. <https://doi.org/10.1067/MOB.2002.126643>.
18. Huang, Jack Y.J., Togas Tulandi, Hananel Holzer, Seang Lin Tan, and Ri-Cheng Chian. 2008. "Combining Ovarian Tissue Cryobanking with Retrieval of Immature Oocytes Followed by in Vitro Maturation and Vitrification: An Additional Strategy of Fertility Preservation." *Fertility and Sterility* 89 (3): 567–72. <https://doi.org/10.1016/J.FERTNSTERT.2007.03.090>.
19. Kasum, Miro, Lidija Beketić-Orešković, Parvin F Peddi, Slavko Orešković, and Rebecca H Johnson. 2014. "Fertility after Breast Cancer Treatment." *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 173 (February): 13–18. <https://doi.org/10.1016/j.ejogrb.2013.11.009>.
20. Lee, SJ, LR Schover, AH Partridge, P Patrizio - J Clin Oncol, and undefined 2006. n.d. "American Society of Clinical Oncology Recommendations on Fertility Preservation in Cancer Patients." *Fi-Md.Com*. Accessed January 27, 2019. <http://f.i-md.com/medinfo/material/30c/4ea7c54844ae30018c1c630c/4ea7c54944ae30018c1c630f.pdf>.
21. Madrigano, A, L Westphal, I Wapnir - The American Journal of Surgery, and undefined 2007. n.d. "Egg Retrieval with Cryopreservation Does Not Delay Breast Cancer Treatment." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0002961007005351>.
22. McLaren, JF, GW Bates - American journal of obstetrics and gynecology, and undefined 2012. n.d. "Fertility Preservation in Women of Reproductive Age with Cancer." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0002937812008617>.
23. Meirow, D, I Hardan, J Dor, ... E Fridman - Human, and undefined 2008. n.d. "Searching for Evidence of Disease and Malignant Cell Contamination in Ovarian Tissue Stored from Hematologic Cancer Patients." *Academic.Oup.Com*. Accessed January 27, 2019. <https://academic.oup.com/humrep/article-abstract/23/5/1007/647283>.
24. Meirow, D, and J G Schenker. 1995. "Cancer and Male Infertility." *Human Reproduction (Oxford, England)* 10 (8): 2017–22. <http://www.ncbi.nlm.nih.gov/pubmed/8567834>.
25. Munster, PN, AP Moore, ... R Ismail-Khan - Journal of Clinical, and undefined 2012. n.d. "Randomized Trial Using Gonadotropin-Releasing Hormone Agonist Triptorelin for the Preservation of Ovarian Function during (Neo) Adjuvant Chemotherapy For." *Ncbi.Nlm.Nih.Gov*. Accessed January 27, 2019. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3295555/>.
26. Noyes, Nicole, Patty Ann Labella, James Grifo, and Jaime M. Knopman. 2010. "Oocyte Cryopreservation: A Feasible Fertility Preservation Option for Reproductive Age Cancer Survivors." *Journal of Assisted Reproduction and Genetics* 27 (8): 495–99. <https://doi.org/10.1007/s10815-010-9434-3>.
27. Ohl, DA, LJ Wolf, AC Menge, GM Christman, WW Hurd - Fertility and sterility, and undefined 2001. n.d. "Electroejaculation and Assisted Reproductive Technologies in the Treatment of Anejaculatory Infertility." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028201028953>.
28. Ohl, Dana A., Susanne A. Quallich, Jens Sønksen, Nancy L. Brackett, and Charles M. Lynne. 2008. "Anejaculation and Retrograde Ejaculation." *Urologic Clinics of North America* 35 (2): 211–20. <https://doi.org/10.1016/J.UCL.2008.01.014>.

29. Oktay, K, ... I Türkçüoğlu - Reproductive biomedicine, and undefined 2010. n.d. "GnRH Agonist Trigger for Women with Breast Cancer Undergoing Fertility Preservation by Aromatase Inhibitor/FSH Stimulation." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S147264831000129X>.
30. Oktay, K, E Buyuk, O Davis, ... I Yermakova - Human, and undefined 2003. n.d. "Fertility Preservation in Breast Cancer Patients: IVF and Embryo Cryopreservation after Ovarian Stimulation with Tamoxifen." *Academic.Oup.Com*. Accessed January 27, 2019. <https://academic.oup.com/humrep/article-abstract/18/1/90/880435>.
31. Oktay, K, E Buyuk, O Davis, I Yermakova, L Veeck, and Z Rosenwaks. 2003. "Fertility Preservation in Breast Cancer Patients : IVF and Embryo Cryopreservation after Ovarian Stimulation with Tamoxifen" 18 (1): 90–95. <https://doi.org/10.1093/humrep/deg045>.
32. Oktay, Kutluk. 2002. "Evidence for Limiting Ovarian Tissue Harvesting for the Purpose of Transplantation to Women Younger than 40 Years of Age." *The Journal of Clinical Endocrinology and Metabolism* 87 (4): 1907–8. <https://doi.org/10.1210/jcem.87.4.8367>.
33. Oktay, Kutluk, Erkan Buyuk, Natalie Libertella, Munire Akar, and Zev Rosenwaks. 2015. "Fertility Preservation in Breast Cancer Patients : A Prospective Controlled Comparison of Ovarian Stimulation With Tamoxifen and Letrozole for Embryo Cryopreservation" 23 (19): 4347–53. <https://doi.org/10.1200/JCO.2005.05.037>.
34. Parmegiani, L, GE Cognigni, ... S Bernardi - Reproductive, and undefined 2011. n.d. "Efficiency of Aseptic Open Vitrification and Hermetical Cryostorage of Human Oocytes." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S1472648311003646>.
35. Practice Committees of American Society for Reproductive Medicine, and Society for Assisted Reproductive Technology. 2013. "Mature Oocyte Cryopreservation: A Guideline." *Fertility and Sterility* 99 (1): 37–43. <https://doi.org/10.1016/j.fertnstert.2012.09.028>.
36. Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. 2013. "In Vitro Maturation: A Committee Opinion." *Fertility and Sterility* 99 (3): 663–66. <https://doi.org/10.1016/j.fertnstert.2012.12.031>.
37. Quinn, GP, ST Vadapampil, ... BA Bell-Ellison - Social science &, and undefined 2008. n.d. "Patient–Physician Communication Barriers Regarding Fertility Preservation among Newly Diagnosed Cancer Patients." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0277953607004996>.
38. Quinn, GP, ST Vadapampil, ... JH Lee - Journal of clinical, and undefined 2009. n.d. "Physician Referral for Fertility Preservation in Oncology Patients: A National Study of Practice Behaviors." *Researchgate.Net*. Accessed January 27, 2019. [https://www.researchgate.net/profile/Gwendolyn\\_Quinn3/publication/26891727\\_Physician\\_Referral\\_for\\_Fertility\\_Preservation\\_in\\_Oncology\\_Patients\\_A\\_National\\_Study\\_of\\_Practice\\_Behaviors/links/56b88bf208ae3b658a88bbcf.pdf](https://www.researchgate.net/profile/Gwendolyn_Quinn3/publication/26891727_Physician_Referral_for_Fertility_Preservation_in_Oncology_Patients_A_National_Study_of_Practice_Behaviors/links/56b88bf208ae3b658a88bbcf.pdf).
39. Quinn, GP, ST Vadapampil, L King, ... CA Miree - Patient education and, and undefined 2009. n.d. "Impact of Physicians' Personal Discomfort and Patient Prognosis on Discussion of Fertility Preservation with Young Cancer Patients." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0738399109004236>.
40. Rienzi, L, S Romano, L Albricci, ... R Maggiulli - Human, and undefined 2009. n.d. "Embryo Development of Fresh 'versus' Vitrified Metaphase II Oocytes after ICSI: A Prospective Randomized Sibling-Oocyte Study." *Academic.Oup.Com*. Accessed January 27, 2019. <https://academic.oup.com/humrep/article-abstract/25/1/66/694746>.

41. Scaravelli, G, V Vigiliano, JM Mayorga, ... S Bolli - Reproductive, and undefined 2010. n.d. "Analysis of Oocyte Cryopreservation in Assisted Reproduction: The Italian National Register Data from 2005 to 2007." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S1472648310003214>.
42. Signorello, LB, SS Cohen, ... C Bosetti - Journal of the, and undefined 2006. n.d. "Female Survivors of Childhood Cancer: Preterm Birth and Low Birth Weight among Their Children." *Academic.Oup.Com*. Accessed January 27, 2019. <https://academic.oup.com/jnci/article-abstract/98/20/1453/2521835>.
43. Signorello, LB, JJ Mulvihill, DM Green, HM Munro - The Lancet, and undefined 2010. n.d. "Stillbirth and Neonatal Death in Relation to Radiation Exposure before Conception: A Retrospective Cohort Study." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0140673610607520>.
44. Silber, S, N Kagawa, M Kuwayama, R Gosden - Fertility and sterility, and undefined 2010. n.d. "Duration of Fertility after Fresh and Frozen Ovary Transplantation." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028209043325>.
45. Silber, Sherman J., and Roger G. Gosden. 2007. "Ovarian Transplantation in a Series of Monozygotic Twins Discordant for Ovarian Failure." *New England Journal of Medicine* 356 (13): 1382–84. <https://doi.org/10.1056/NEJMc066574>.
46. Smits, J, MM Dolmans, ... J Donnez - Human reproduction, and undefined 2010. n.d. "Current Achievements and Future Research Directions in Ovarian Tissue Culture, in Vitro Follicle Development and Transplantation: Implications for Fertility Preservation." *Academic.Oup.Com*. Accessed January 27, 2019. <https://academic.oup.com/humupd/article-abstract/16/4/395/800184>.
47. Sonmezer, Murat, and Kutluk Oktay. 2010. "Orthotopic and Heterotopic Ovarian Tissue Transplantation." *Best Practice & Research Clinical Obstetrics & Gynaecology* 24 (1): 113–26. <https://doi.org/10.1016/J.BPOBGYN.2009.09.002>.
48. sterility, Practice Committee of the American Society for - Fertility and, and undefined 2013. n.d. "Recommendations for Gamete and Embryo Donation: A Committee Opinion." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S001502821202256X>.
49. Terenziani, M, L Piva, C Meazza, L Gandola, G Cefalo - Fertility and sterility, and undefined 2009. n.d. "Oophorectomy: A Relevant Role in Preservation of Ovarian Function after Pelvic Irradiation." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028208039319>.
50. "Testing and Interpreting Measures of Ovarian Reserve: A Committee Opinion." 2012. *Fertility and Sterility* 98 (6): 1407–15. <https://doi.org/10.1016/J.FERTNSTERT.2012.09.036>.
51. Tulandi, T, S Al-Took - Fertility and sterility, and undefined 1998. n.d. "Laparoscopic Ovarian Suspension before Irradiation." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028298001551>.
52. Wolff, M von, CJ Thaler, T Frambach, C Zeeb - Fertility and sterility, and undefined 2009. n.d. "Ovarian Stimulation to Cryopreserve Fertilized Oocytes in Cancer Patients Can Be Started in the Luteal Phase." *Elsevier*. Accessed January 27, 2019. <https://www.sciencedirect.com/science/article/pii/S0015028208033670>.
53. Zinger, M, JH Liu, ... N Husseinzadeh - The Journal of, and undefined 2004. n.d. "Successful Surrogate Pregnancy after Ovarian Transposition, Pelvic Irradiation and Hysterectomy." *Europepmc.Org*. Accessed January 27, 2019. <https://europepmc.org/abstract/med/15305832>.